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Review Article

# A Note on Relative Potency Theorem

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**Abstract**

In this work, further relative potency properties and a thorough proof have been attained. The findings are derived using the Taylor's (Maclaurin's) series, and the expected value and variance of the relative potency are as a consequence. Alternately, the first and second moment for the relative potency (R)are obtained given the potency.

## Introduction

The common assumption is that the test doses and the standard doses have the same variance and follow two normal distributions (Bivariate Normal Distribution) [1]. Suppose we have $\{X_{T1}, X_{T2}, X_{T3} \dots X_{nT}\}$ which are identical and independently distributed N() and $\{X_{S1}, X_{S3}, X_{S3}, \dots, X_{nS}\}$ are also identical and independently distributed and N(), where $\rho = \mu_S / \mu_T$ is estimated by $R = \frac{\bar{x}_S}{\bar{x}_T}$.

where: $n_s$ is the number of subjects assigned to the standard preparation

$n_T$ is the number of subjects assigned to the test preparation.

$X_{Si}$ is the Individual Effect Dose (IED) of the $i^{th}$ subject receiving the standard preparation.

$X_{Tj}$ is the IED of the $j^{th}$ subject receiving the test preparation.

The proof and other properties (first and second moments) have not been fully explained in the literature. Hence the need to address these.

**Proof**: Let $\{X_{Si} : i = 1, \dots, n_s\}$ be a random sample from a population (not necessarily normal) with mean and variance while $\{X_{Ti} : i = 1, \dots, n_T\}$ is a random sample from a population (not necessarily normal) with mean and variance where the samples are independent. Then if and ρ = /, we have E(R) ρ and var(R) = $\frac{\sigma^2}{\mu_T^2}\left\{\frac{1}{n_S} + \frac{\rho^2}{n_T}\right\}$

**Note:** R is a ratio of two random variables and so its expected value is not $E(\bar{X}_S)\ /\ E(\bar{X}_T)$

we have $E(R) \cong \rho$ and $var(R) = \frac{\sigma^2}{\mu_T^2}\left\{\frac{1}{n_S} + \frac{\rho^2}{n_T}\right\}$

**Note:** R is a ratio of two random variables and so its expected value is not $E(\bar{X}_S)\ /\ E(\bar{X}_T)$

ie $ER \neq E(\bar{X}_S) / E(\bar{X}_T)$

**Proof**: The following results can be derived from the Taylor's (Maclaurin's) series.

If $f(x,y) = f(a,b) + (x - a) + (y - b) + \dots$ (1)

where expansion is about x = a and y = b.

Let R = relative potency of the sample

$$\rightarrow R = R(\bar{X}_S, \bar{X}_T) = \frac{\bar{X}_S}{\bar{X}_T} \quad (2)$$

$$\text{and } R(\bar{X}_S, \bar{X}_T) = f(\bar{X}_S, \bar{X}_T) + (\bar{X}_S - \mu_S)\frac{\partial Y}{\partial \bar{x}_S} + (\bar{X}_T - \mu_T)\frac{\partial Y}{\partial \bar{x}_T} + \dots \quad (3)$$

$$\frac{\partial R}{\partial \bar{x}_S} = \frac{1}{\bar{x}_T} \ and \ \frac{\partial R}{\partial \bar{x}_T} = \frac{-\bar{x}_S}{\bar{x}_T^2}$$

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$$\therefore \; R = \frac{\mu_S}{\mu_T} + (\bar{X}_S - \mu_S)\left(\frac{1}{\mu_T}\right) + (\bar{X}_T - \mu_T)\left(\frac{-\mu_S}{\mu_T^2}\right) + \cdots$$

$$\rightarrow E(R) = E\left(\frac{\bar{X}_S}{\mu_T}\right) - E\left(\frac{\mu_S \bar{x}_T}{\mu_T^2}\right) + E\left(\frac{\mu_S}{\mu_T}\right)$$

$$= \frac{1}{\mu_T} E(\bar{X}_S) - \frac{\mu_S}{\mu_T^2} E(\bar{X}_T) + \frac{\mu_S}{\mu_T}$$

$$E(R) = \frac{\mu_S}{\mu_T} - \frac{\mu_S \mu_T}{\mu_T^2} + \frac{\mu_S}{\mu_T} = \frac{\mu_S}{\mu_T} \cdot \frac{\mu_S}{\mu_T} + \frac{\mu_S}{\mu_T}$$

$$\rightarrow E(R) \cong \frac{\mu_S}{\mu_T} = \rho$$

$$E(R) \cong \rho \; \rightarrow R \; (unbiased\ estimator\ of\ \rho)$$

$\rho = \mu_S/\mu_T$ $and$ $R = \frac{\bar{x}_S}{\bar{x}_T}$; $E(R) \cong \rho$ where $\rho$ is potency and $R$ is the relative potency

$$\rightarrow Var(R) = Var\left(\frac{\mu_S}{\mu_T}\right) + \left(\frac{1}{\mu_T}\right)^2 Var(\bar{X}_S - \mu_S) + \left(\frac{-\mu_S}{\mu_T^2}\right)^2 Var(\bar{X}_T - \mu_T)$$

$but\ V(k) = 0,\quad Var(z-k) = Var(z), where\ k\ is\ a\ constant\ and\ z\ is\ a\ r.v$

$$\rightarrow Var(R) = 0 + \frac{1}{\mu_T^2}\; V(\bar{X}_S) + \frac{\mu_S^2}{\mu_T^4} V(\bar{X}_T).$$

$$Var\ (R) = \frac{1}{\mu_T^2}\left\{V(\bar{X}_S) + \frac{\mu_S^2}{\mu_T^2} V(\bar{X}_T)\right\}$$

$$but\ \rho = \frac{\mu_S}{\mu_T} \;\rightarrow \rho^2 = \frac{\mu_S^2}{\mu_T^2}, \text{also, } V(\bar{X}_S) = \frac{\sigma^2}{n_S}\ and\ V(\bar{X}_T) = \frac{\sigma^2}{n_T}$$

$$Var\ (R) \cong \frac{1}{\mu_T^2}\left\{\frac{\sigma^2}{n_S} + \rho^2 \frac{\sigma^2}{n_T}\right\} \cong \frac{\sigma^2}{\mu_T^2}\left\{\frac{1}{n_S} + \frac{\rho^2}{n_T}\right\}$$

$$Also, from\ \ R \cong \frac{\mu_S}{\mu_T} + (\bar{X}_S - \mu_S)\left(\frac{1}{\mu_T}\right) + (\bar{X}_T - \mu_T)\left(\frac{-\mu_S}{\mu_T^2}\right)$$

$$R \cong \frac{\mu_S}{\mu_T} + \frac{\bar{X}_S}{\mu_T} - \frac{\mu_S}{\mu_T} - \frac{\bar{X}_T}{\mu_T^2}\mu_S + \frac{\mu_S \mu_T}{\mu_T^2}$$

$$R = \frac{\bar{x}_S}{\mu_T} - \frac{\mu_S \bar{x}_T}{\mu_T^2} + \frac{\mu_S}{\mu_T}$$

**Corollary** : Given that the populations in the Theorem above is normal, then $\sqrt{n_S(R-\rho)} \cong N\left[0, \frac{\sigma^2}{\mu_T^2}\left(1 + \frac{n_T}{n_S}\rho^2\right)\right]$

**Remark**

**a. Homogeneity of Variance:** For ease of comparison, the variance of the two preparations is assumed to be equal. To test this assumption, we use the F-distribution, where $n_S - 1$ is the numerator degree of freedom and $n_T - 1$ is the denominator degree of freedom [2].

$$F_{cal} = \frac{S_S^2}{S_T^2}$$

where and are the sample variances of the standard and test preparations respectively.

**b. Variance Estimate:** Following from Theorem above,

$$\mathrm{Var}(R) \cong \frac{\sigma^2}{\mu_T^2}\left\{\frac{1}{n_S} + \frac{\rho^2}{n_T}\right\}$$

$$SE(R) \cong \frac{S_p}{X_T}\sqrt{\left\{\frac{1}{n_S} + \frac{r^2}{n_T}\right\}}$$

$s_P^2 = \frac{(n_{S-1})S_S^2 + (n_{T-1})S_T^2}{n_{S+}n_{T-2}}$; where $s_P^2$ is the pooled variance.

Establishing the Moment Generating Function for the relative potency, R.

Given $R = \frac{x}{y}$

$$\ln R = \ln x - \ln y$$

$$\mathrm{E}(\ln R) = \mathrm{E}(\ln x) - \mathrm{E}(\ln y)$$

$$\ln x = \sum_{n=1}^{\infty}(-1)^{n-1}\frac{(x-1)^n}{n}$$

$$\ln y = \sum_{n=1}^{\infty}(-1)^{n-1}\frac{(y-1)^n}{n}$$

$$\mathrm{E}(\ln x) = \sum_{n=1}^{\infty}\frac{(-1)^{n-1}}{n}\mathrm{E}(x-1)^n$$

$$\mathrm{E}(\ln y) = \sum_{n=1}^{\infty}\frac{(-1)^{n-1}}{n}\mathrm{E}(y-1)^n$$

$$\mathrm{E}\ln x - \mathrm{E}\ln y = \sum_{n=1}^{\infty}\frac{(-1)^{n-1}}{n}\mathrm{E}[(x-1)^n - (y-1)^n]$$

$$(x-1)^n = \sum_{i=0}^{n}\begin{bmatrix} n \\ i \end{bmatrix} x^{n-i}(-1)^i = x^n - \sum_{i=1}^{n}$$

$$(y-1)^n = \sum_{i=0}^{n}\begin{bmatrix} n \\ i \end{bmatrix} y^{n-i}(-1)^i$$

$$(x-1)^n = \sum_{i=0}^{n}\begin{bmatrix} n \\ i \end{bmatrix} x^{n-i}(-1)^i = x^n + \sum_{i=1}^{n-1} x^{n-i}(-1)^i + (-1)^n$$

$$x^n + (-1)^n + \sum_{i=1}^{n-1} x^{n-i}(-1)^i$$

$$y^n + (-1)^n + \sum_{i=1}^{n-1} y^{n-i}(-1)^i$$

$$x^n - y^n + (-1)^n \sum_{i=1}^{n-1}(x^{n-i} - y^{n-i})\begin{bmatrix} n \\ i \end{bmatrix}$$

$$\mathrm{E}\ln x - \mathrm{E}\ln y = \sum_{n=1}^{\infty}\frac{(-1)^{n-1}}{n}\mathrm{E}[(x-1)^n - (y-1)^n]$$

$$= \sum_{n=1}^{\infty}\frac{(-1)^{n-1}}{n}\mathrm{E}\left[x^n - y^n + \sum_{i=1}^{n-1}\begin{bmatrix} n \\ i \end{bmatrix}(x^{n-i} - y^{n-i})\right]$$

$$= \sum_{n=1}^{\infty}\frac{(-1)^{n-1}}{n}\left[\mathrm{E}(x^n) - \mathrm{E}(y^n) + \sum_{i=1}^{n-1}\begin{bmatrix} n \\ i \end{bmatrix}(\mathrm{E}(x^{n-i}) - \mathrm{E}(y^{n-i}))\right]$$

$$\sum_{n=1}^{\infty}\frac{(-1)^{n-1}}{n}\left(\mu_n(x) - \mu_n(y) + \sum_{i=1}^{n-1}\begin{bmatrix} n \\ i \end{bmatrix}[\mu_{n-i}(x) - \mu_{n-i}(y)]\right)$$

where

$$\mu^n = \sum_{n=1}^{n}\frac{(-1)^{n-1}}{n}\left(\mu_n(x) - \mu_n(y) + \sum_{i=1}^{n-1}\begin{bmatrix} n \\ i \end{bmatrix}[\mu_{n-i}(x) - \mu_{n-i}(y)]\right)$$

$$\mu^1 = \sum_{n=1}^{n=1}\frac{1}{n}(\mu_1(x) - \mu_1(y)) = \mu_1(x) - \mu_1(y) = \mu(x) - \mu(y)$$

$$\mu^2 = \sum_{n=1}^{n=2} \frac{(-1)^{1-1}}{n} \left( \mu_n(x) - \mu_n(y) + \sum_{i=1}^{n-1} \begin{bmatrix} n \\ i \end{bmatrix} [\mu_{n-i}(x) - \mu_{n-i}(y)] \right)$$

$$\mu^2 = \mu(x) - \mu(y) + -\frac{1}{n} \left( \mu_2(x) - \mu_2(y) + \sum_{i=1}^{n-1} \begin{bmatrix} n \\ i \end{bmatrix} [\mu_{n-i}(x) - \mu_{n-i}(y)] \right)$$

$$\mu^2 = \mu(x) - \mu(y) - \frac{1}{n} [\mu_2(x) - \mu_2(y)]$$

$$\mu^2 = \mu(x) - \frac{1}{n} \mu_2(x) - \mu(y) + \frac{1}{n} \mu_2(y)$$

$$= \mu(x) - \frac{\mu_2(x)}{n} + \frac{1}{n} \mu_2(y) - \mu(y)$$

## Conclusion

A detailed proof and other properties of relative potency have been established, hence, certain other expression; the coefficient of variation, skewness and kurtosis can be obtained [3].

## References


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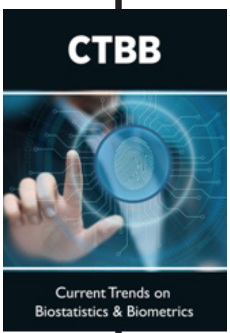


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