

Systematic Bioinformatics Review and *In Silico* Analysis of REDOXX®

ABSTRACT

The systematic bioinformatics review and *in silico* analysis of REDOXX® was performed to integrate over 3,000 *in vitro* and *in vivo* laboratory experiments recorded in 94 studies that were conducted across 64 institutions over the past 36 years. The analysis reveals two (2) mechanisms of action involved in immune function at the molecular systems level in humans. The *in silico* results reveal that four (4) active ingredients in REDOXX were synergistically efficacious in affecting three (3) biomarkers associated with immune function.

KEY FINDINGS

1. CytoSolve® *in silico* analysis identified and computationally modeled two (2) major biomolecular processes involved in immune function:
 - a. TLR-4 signaling pathway
 - b. IL-6 signaling pathway
2. Bioactive compounds in REDOXX were found to have a positive synergistic effect on both biomolecular processes involved in immune function.
3. REDOXX improved immune function by downregulating TLR-4 signaling pathway and downregulating IL-6 signaling pathway.
4. The combination of ingredients in REDOXX affect three (3) biomarkers of immune function, TNF- α , PDL-1 and IL-6, as follows:
 - a. **Epicatechin, procyanidin B1 and procyanidin B2** from grape seed extract inhibit NF-kB activation leading to suppression of IL-6, and TNF- α expression in TLR-4 signaling pathway.
 - b. **Vitamin A, and Quercetin** inhibit NF-kB activation leading to suppression of IL-6, and TNF- α expression in TLR-4 signaling pathway.
 - c. **Gingkolide A1** from Gingko biloba leaf extract inhibits STAT3 activation leading to suppression of PDL-1 expression in IL-6 signaling pathway.
 - d. **Epicatechin and procyanidin B** in grape seed extract inhibit STAT3 activation leading to suppression of PDL-1 expression in IL-6 signaling pathway.
 - e. **Quercetin** inhibits gp130 phosphorylation leading to suppression of PDL-1 expression in IL-6 signaling pathway.

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