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In Vitro and In Silico Study of Cytotoxicity of Metal Oxide Nanoparticles towards Escherichia coli

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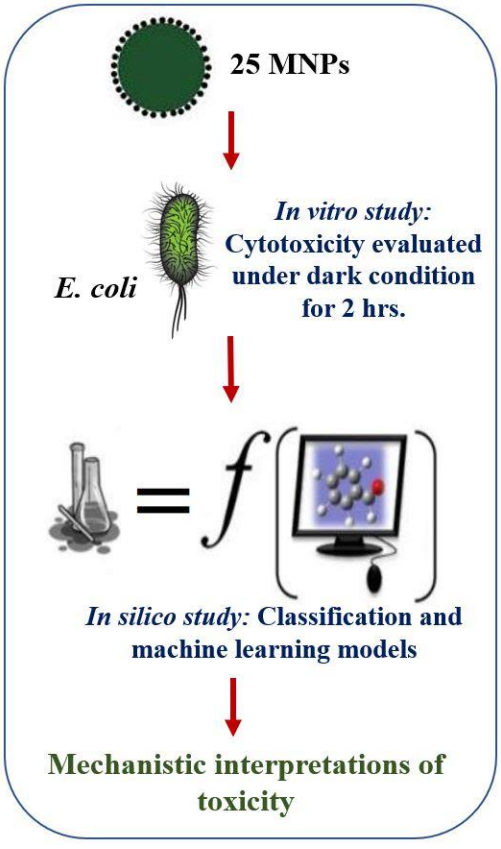
Graphical Abstract



Abstract.

In continuation of study of 17 metal oxide nanoparticles (MNPs) cytotoxicity to E. coli after 2 hrs. exposure under dark conditions, we have evaluated cytotoxicity of additional 8 MNPs maintaining equivalent experiemental conditions following the literature (1). The overall cytotoxicity ranking of these additional MNPs according to LC_{50} values in descending order is Er_2O_3, Gd_2O_3, CeO_2, Co_2O_3, Mn_2O_3, Co_3O_4, Fe_3O4/WO_3. The in vitro study clearly suggested that Er_2O_3 and Gd_2O_3 are the most toxic among all 25 MNPs under the mentioned experiemental conditions. The present experiemental data is one of the biggest available nano metal oxide cytotoxicity data for E. coli at present time performed under similar experimental conditions and same laboratory. Therefore, the obtained data is significant in terms of OECD principle 1 of defined endpoint to develop statistically acceptable and predictive in silico models. As two MNPs, WO_3 and Fe_3O_4 did not show toxicity even at 2000 ppm, the highest tested concentration in this study we can't quantify the toxicity data for these two specific MNPs. On the other hand, Er_2O_3 and Gd_2O_3 showed significantly higher toxicity value compare to remaining metal oxides which make them influential data points for the in silico studies. In this background, we have considered a comprehensive approach that includes a total of seven classification and machine learning algorithms i.e. linear discriminant

	analysis (LDA), naïve bayes, multinomial logistic regression, Sequential minimal optimization (SMO), AdaBoost, J48 and random forest to model all 25 MNPs to understand and identify the major mechanism for such toxicities (2,3) without excluding any MNPs. To correlate the toxicity employing the in silico tools, we have employed 1st (4) and 2nd (5) generation periodic table descriptors developed by us which can be computed in no time without any sophisticated computing facilities. Among the seven models, the LDA based model emerged as the best model considering goodness-of-fit and prediction capability checked on training ($N_{Training}$=17) and test set (N_{Test}=8). The electronegativity count of oxygen and the core environment of metal defined by the ratio of the number of core electrons to the number of valence electrons showed positive contributions towards toxicity. The identification of these molecular descriptors may be beneficial in explaining the mechanisms of nanotoxicity and for predicting the environmental risk associated with release of the MNPs. The developed models can be resourcefully employed for environmental risk assessment tools for the E. coli for any new/untested MNPs along with the influence in the future design and manufacture of safe nanomaterials.

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