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**RESEARCH ARTICLE**

# Acute toxicity prediction of synthetic and natural preservatives in rat by using QSAR modeling software

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## *Abstract*

Preservatives are chemicals that prevent spoiling the foods from bacteria and fungi. These chemicals are of artificial or natural origin. The present study aims acute toxicity prediction as $LD_{50}$ (median lethal dose) values of synthetic/artificial and natural preservatives in rat by oral exposure. The predictions of $LD_{50}$ values were determined by using T.E.S.T. (Toxicity Estimation Software Tool) for these common preservatives used in raw and/or processed foods. Among the selected 16 synthetic and natural preservatives, predictive $LD_{50}$ values by T.E.S.T. were obtained only in 8 artificial compounds while for natural preservatives, out of 16 compounds 15 nos. were obtained. The predicted $LD_{50}$ values for synthetic compounds viz. benzoic acid, ethyl *para*-hydroxybenzoate, lactic acid, propionic acid, sorbic acid, butylated hydroxytoluene, butylated hydroxyanisole and formaldehyde were observed but potassium sorbate, sodium benzoate, calcium benzoate, sodium propionate, disodium EDTA, sodium gallate, nitrite and sulphite unable to predict the $LD_{50}$ values due to unidentified CAS no. in database while for natural compounds viz. caffeic acid, cinnamic acid, ferulic acid, gallic acid, oleuropein, thymol, eugenol, ascorbic acid, tartaric acid, malic acid, fumaric acid, tocopherol acetate, carvacrol, citral and allin were obtained. It was observed from the prediction by the T.E.S.T. that synthetic preservatives are moderately toxic except formaldehyde and propionic acid, these 2 are very toxic while natural preservatives are only moderately toxic and lactic acid is slightly toxic. This software helps to predict of $LD_{50}$ values by easy screening. It is also suggested to compare the predicted data with other available related softwares and natural preservatives may suitable compared to artificial preservatives.



## INTRODUCTION

Preservatives are chemical compounds that can originate from both artificial and natural source. The functions of artificial and natural preservatives in food substances are mainly killing the growth of microorganisms such as bacteria and fungi (Soeda et al., 1966; CAL, 1988; Cutler, 1995; Puupponen et al., 2001; Erasto et al., 2004; Souza et al., 2005; Mohanka and Priyanka, 2014). The artificial or synthetic preservatives have formed by several chemical reactions but the natural preservatives can directly be obtained from plant and/or animal origin, which are known as bioactive compounds. It has already been established the physical and chemical nature, mode of actions etc. of both artificial as well as natural chemical compounds used as preservative in food to prevent spoilage from bacteria and

fungi (Close and Nielsen, 1976; Chapman, 1998; Nararasimhan et al., 2003; Narasimhan et al., 2004; Ou and Kwok, 2004; Bhullar et al., 2013; Mohanka and Priyanka, 2014).

In new research era, quantitative structure–activity relationship (QSAR) is logic based mathematical simulation of the structure-derived features of a chemical compound and their relation with biological or physicochemical activity already established for one or more than one chemical as preservative (Narasimhan and Dhake, 2006; Narasimhan et al., 2006; Chaudhary et al., 2008; Narasimhan et al., 2009; Roy et al., 2011; Sarova et al., 2011; Mahiwal et al., 2012). QSAR modeling helps to predict several biological activity viz. acute toxicity, mutagenicity, developmental toxicity etc. or inhibitory versus non-inhibitory activities of compound(s) prior to bioassay. The established molecular descriptors have been used to determine the exact prediction of chemical(s). Generally the molecular descriptors are used on the basis of three parameters viz. thermodynamic, steric and electronic (Choplin, 2005; Valentina et al., 2009) in QSAR modeling. In T.E.S.T., the parameters also include E-state values and E-state counts, constitutional descriptors, topological descriptors, walk and path counts, connectivity, information content, 2D autocorrelation, Burden eigenvalue, molecular property (such as the octanol-water partition coefficient), Kappa, hydrogen bond acceptor/donor counts, molecular distance edge, and molecular fragment counts (Cassano et al., 2010; USEPA, 2012).

The bioassay with animals for any compound is difficult to get data within a short duration, need more expenditure and time-consuming, presently some restrictions to use animal species by the regulatory authorities. In this context, the toxicity prediction has been postulated through QSAR along with statistical modeling (Zhu et al., 2009), which is a computer based suitable technique (Worth et al., 2007; Patil et al., 2014). Scattered works on toxicity prediction by using QSAR modeling have been reported for preservatives from artificial as well as natural origin (Narasimhan et al., 2003; 2004; 2006; Chaudhary et al., 2008; Venkataramana et al., 2011; Mahiwal et al., 2012).

It has already been recommended several toxicity prediction softwares by many researchers (Pallas, Compu Drug International Inc., 2000; TOPKAT, 2004; Talete, 2006; User manual (ADMET), Simulation Plus Inc, 2011; USEPA, 2012). Among all these softwares, the T.E.S.T. (Toxicity Estimation Software Tool) by USEPA (2012) is a non-commercial software and easy to operate for obtaining predictive values within short period of time (Ruiz et al., 2002; Talapatra et al., 2015). In this package, it was found QSAR modeling to calculate the toxicity of chemical(s) using suitable molecular descriptors along with statistical interpretation.

In the T.E.S.T software, multiple prediction methodologies have been incorporated, which has higher confidence level in the toxicity prediction (the values for predicted toxicities are closely related from different methods). In addition, particular QSAR approaches depend upon the confidence at higher level by individual experience of researchers (USEPA, 2012).

In this present study an attempt has been made to predict acute toxicity as $LD_{50}$ values of artificial and natural chemicals found in preservatives in the rat orally exposed through QSAR modeling software package T.E.S.T.

## MATERIALS AND METHODS

In the present study, established 16 types of synthetic and natural preservatives were selected based on the usage in raw and processed food items. The present study was emphasized to estimate the $LD_{50}$ values of synthetic and natural preservatives through QSAR modeling software package (T.E.S.T., Verson 4.1) in rat oral exposure (US EPA, 2012) and this easy screening software was used for acute toxicity prediction. The value for acute toxicity study was tabulated after obtaining predictive value of individual compound from T.E.S.T. software. It was studied the $LD_{50}$ data from a consensus method, which is basically the average predicted $LD_{50}$ value calculated from other inbuilt QSAR methodologies viz. hierarchical clustering method, the FDA MDL method and nearest neighbor methods (Martin et al., 2008; USEPA, 2012). In T.E.S.T., the structure of studied chemical can only be visualized when entering CAS no. of individual chemical by clicking on calculate option. The predicted value of consensus method can only be obtained after processing the software. This software is programmed by the inbuilt of 7,420 chemicals' database (Martin et al., 2008) and is only based on 2-dimensional molecular descriptors of 797 nos. (Zhu et al., 2009; USEPA, 2012).

In T.E.S.T., it is prescribed that the $R^2$ (correlation coefficient) value if shows greater than 60% then the prediction data is reliable and the predictive ability of each of the QSAR methodologies is evaluating by statistical external validation (Golbraikh and Tropsha, 2002; Golbraikh et al., 2003; Gramatica and Pilutti, 2004; Zhu et al., 2009). According to Zhu et al. (2009), the applicability domain (AD) is calculated for each method to justify exact prediction. The AD is based on the correct validation of predictive activity in T.E.S.T. (USEPA, 2012). It was known that the QSAR modeling can only predict the potential toxicity of any chemical but the confidence level in such predictions can vary (USEPA, 2012). However, in the QSAR model ADs, the features and limitations can be

understood in detail after suitable interpretation of predictions (Golbraikh and Tropsha, 2002; Golbraikh et al., 2003; Netzeva et al., 2005; Schultz et al., 2007; Tropsha and Golbraikh, 2007; Tetko et al., 2008; Zhu et al., 2009; Roy et al., 2011; Ruiz et al., 2012). The predictive value for acute toxicity with special reference to $LD_{50}$ values in rat after orally exposed to artificial and natural preservatives were only determined by using QSAR modeling T.E.S.T. software (USEPA, 2012).

## RESULTS

In Table – 1, the acute toxicity prediction data were tabulated for both artificial and natural preservatives and these compounds were selected along with their CAS (Chemical Abstracts Services) no. Out of the 16 artificial preservatives, the predicted values of $LD_{50}$ (mg/kg) were obtained by using T.E.S.T. of only 8 compounds viz. benzoic acid (1180.99), ethyl *para*-hydroxybenzoate (2695.96) lactic acid (4723.98), propionic acid (475.28), sorbic acid (1873.12), butylated hydroxytoluene (1639.84), butylated hydroxyanisole (1475.73) and formaldehyde (85.97). Other 8 compounds viz. potassium sorbate, sodium benzoate, calcium benzoate, sodium propionate, disodium EDTA, sodium gallate, sodium nitrite and sodium sulphite unable to predict the $LD_{50}$ values due to CAS no. was not identified by the software.

It was also observed that out of the 16 natural preservatives, the predicted values of $LD_{50}$ (mg/kg) were determined by using T.E.S.T. of 15 compounds viz. caffeic acid (2109.96), cinnamic acid (1817.89), ferulic acid (4742.73), gallic acid (3912.42), oleuropein (4101.86), thymol (714.92), eugenol (2138.45), ascorbic acid (14329.94), tartaric acid (4117.91), malic acid (2600.88), fumaric acid (1000.03), tocopherol acetate (4047.66), carvacrol (1018.17), citral (3022.51) and allin (1502.43). Only 1 compound namely citric acid unable to predict the $LD_{50}$ values due to CAS number was not identified by the software (Table – 1).

All the predicted chemicals for both artificial and natural compounds were very well expressed in the model database by the statistical analysis as per FDA cluster model fit results were tabulated (Table – 1). In this software, the similarity analysis was showed very close similarity with other for related chemicals. The predicted value along with statistically significant value ($R^2$ and $Q^2$) for individual chemical was obtained by T.E.S.T. and individual data of chemical from FDA model result for artificial (Fig. 1, 2, 3, 4, 5, 6, 7 and 8) and natural (Fig. 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22 and 23) preservatives were represented graphically.

**Table 1. QSAR prediction of acute toxicity ($LD_{50}$) in rat at oral exposure for synthetic and natural preservatives by using T.E.S.T. software**

| Sl. No. | Synthetic preservatives | CAS No. | Predicted $LD_{50}$ (mg/kg) | Natural preservatives | CAS No. | Predicted $LD_{50}$ (mg/kg) |
|---|---|---|---|---|---|---|
| 1. | Potassium sorbate | 24634-61-5 | n.f. | Caffeic acid | 331-39-5 | 2109.96 |
| 2. | Sodium benzoate | 532-32-1 | n.f. | Cinnamic acid | 140-10-3 | 1817.89 |
| 3. | Calcium benzoate | 2090-05-3 | n.f. | Ferulic acid | 1135-24-6 | 4742.73 |
| 4. | Benzoic acid | 65-85-0 | 1180.99 | Gallic acid | 149-91-7 | 3912.42 |
| 5. | Ethyl *para*- hydroxybenzoate | 120-47-8 | 2695.96 | Oleuropein | 32619-42-4 | 4101.86 |
| 6. | Lactic acid | 50-21-5 | 4723.98 | Thymol | 89-83-8 | 714.92 |
| 7. | Sodium propionate | 137-40-6 | n.f. | Eugenol | 97-53-0 | 2138.45 |
| 8. | Propionic acid | 79-09-4 | 475.28 | Citric acid | 5949-29-1 | n.f. |
| 9. | Sorbic acid | 110-44-1 | 1873.12 | Ascorbic acid | 50-81-7 | 14329.94 |
| 10. | Disodium EDTA | 6381-92-6 | n.f. | Tartaric acid | 87-69-4 | 4117.91 |
| 11. | Butylated hydroxytoluene | 128-37-0 | 1639.84 | Malic acid | 6915-15-7 | 2600.88 |
| 12. | Butylated hydroxyanisole | 25013-16-5 | 1475.73 | Fumaric acid | 110-17-8 | 1000.03 |
| 13. | Sodium gallate | 2053-21-6 | n.f. | Tocopherol acetate | 58-95-7 | 4047.66 |
| 14. | Sodium nitrite | 7632-00-0 | n.f. | Carvacrol | 499-75-2 | 1018.17 |
| 15. | Sodium sulphite | 7757-83-7 | n.f. | Citral | 5392-40-5 | 3022.51 |
| 16. | Formaldehyde | 50-00-0 | 85.97 | Allin | 556-27-4 | 1502.43 |

n.f. = Not found in T.E.S.T.

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.856 |
| $q^2$ | 0.764 |
| #chemicals | 30 |
| Model | FDA Model |

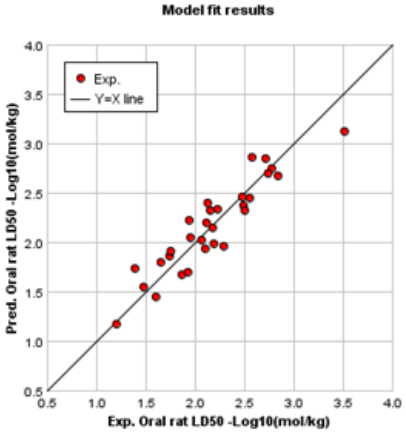


**Fig. 1. Statistical analysis and graph for benzoic acid prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.814 |
| $q^2$ | 0.724 |
| #chemicals | 44 |
| Model | FDA Model |

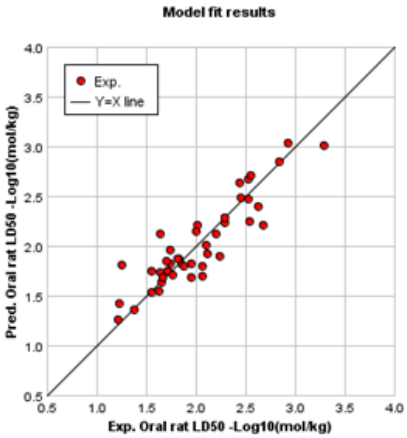


**Fig. 2. Statistical analysis and graph for ethyl *para*-hydroxybenzoate prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.899 |
| $q^2$ | 0.835 |
| #chemicals | 34 |
| Model | FDA Model |

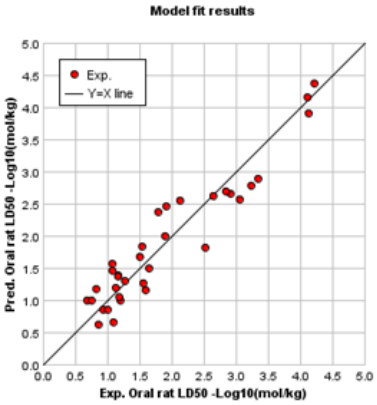


**Fig. 3. Statistical analysis and graph for lactic acid prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.824 |
| $q^2$ | 0.737 |
| #chemicals | 30 |
| Model | FDA Model |

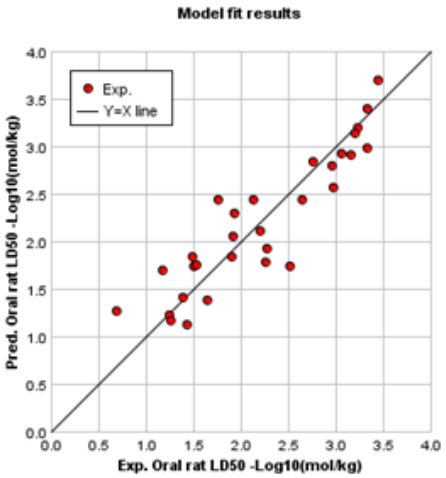


**Fig. 4. Statistical analysis and graph for propionic acid prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.703 |
| $q^2$ | 0.567 |
| #chemicals | 35 |
| Model | FDA Model |

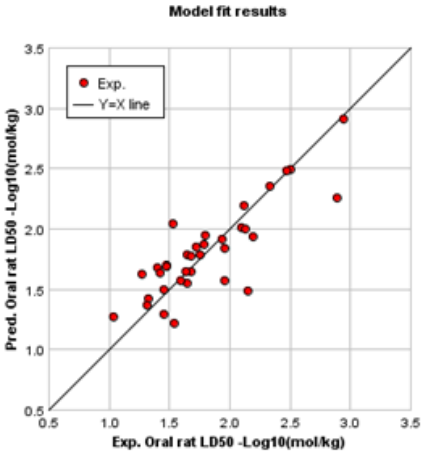


**Fig. 5. Statistical analysis and graph for sorbic acid prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.727 |
| $q^2$ | 0.557 |
| #chemicals | 35 |
| Model | FDA Model |

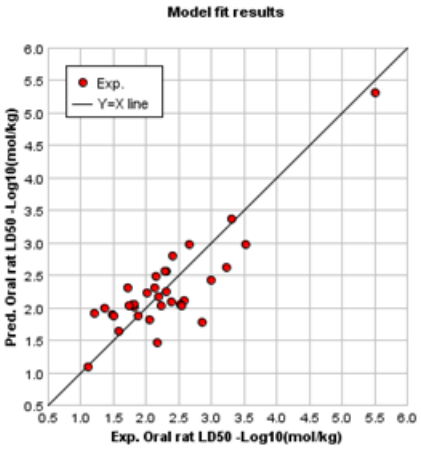


**Fig. 6. Statistical analysis and graph for butylated hydroxytoluene prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.762 |
| $q^2$ | 0.626 |
| #chemicals | 30 |
| Model | FDA Model |

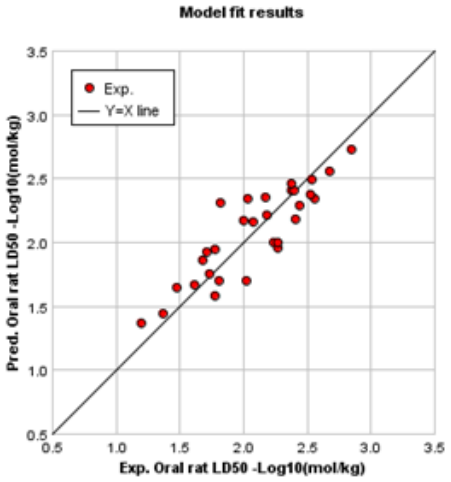


**Fig. 7. Statistical analysis and graph for butylated hydroxyanisole prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.876 |
| $q^2$ | 0.840 |
| #chemicals | 29 |
| Model | FDA Model |

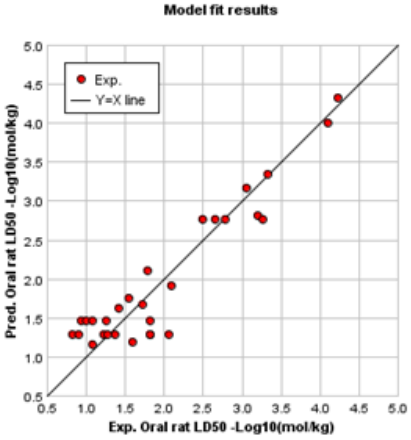


**Fig. 8. Statistical analysis and graph for formaldehyde prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.949 |
| $q^2$ | 0.902 |
| #chemicals | 30 |
| Model | FDA Model |

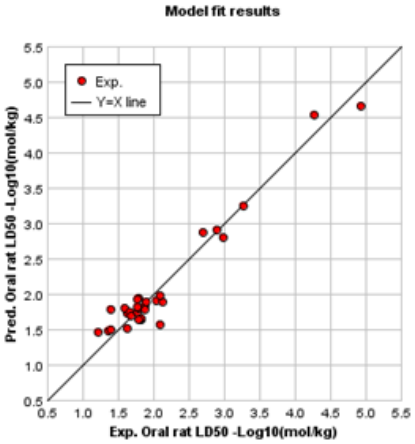


**Fig. 9. Statistical analysis and graph for caffeic acid prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.885 |
| $q^2$ | 0.772 |
| #chemicals | 30 |
| Model | FDA Model |

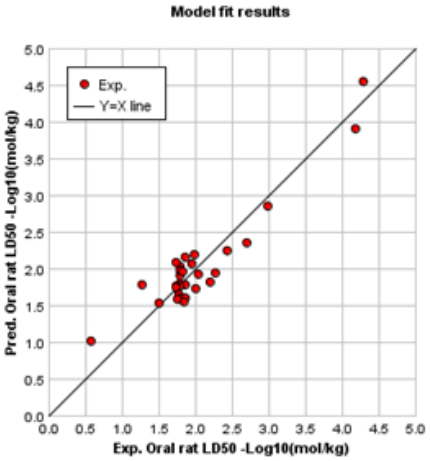


**Fig. 10. Statistical analysis and graph for cinnamic acid prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.922 |
| $q^2$ | 0.875 |
| #chemicals | 40 |
| Model | FDA Model |

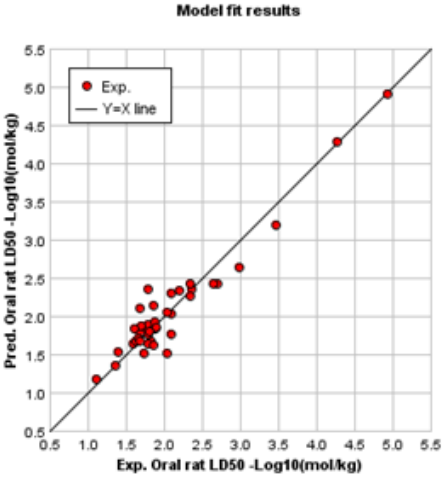


**Fig. 11. Statistical analysis and graph for ferulic acid prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.838 |
| $q^2$ | 0.671 |
| #chemicals | 30 |
| Model | FDA Model |

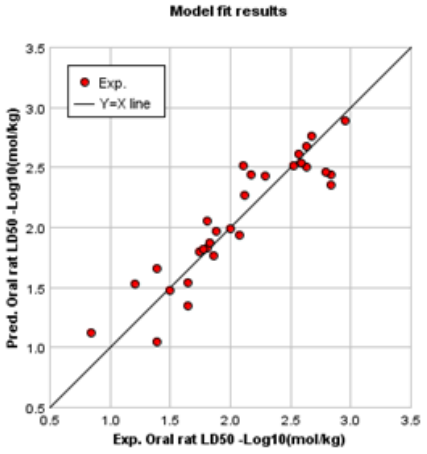


**Fig. 12. Statistical analysis and graph for gallic acid prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.809 |
| $q^2$ | 0.682 |
| #chemicals | 30 |
| Model | FDA Model |

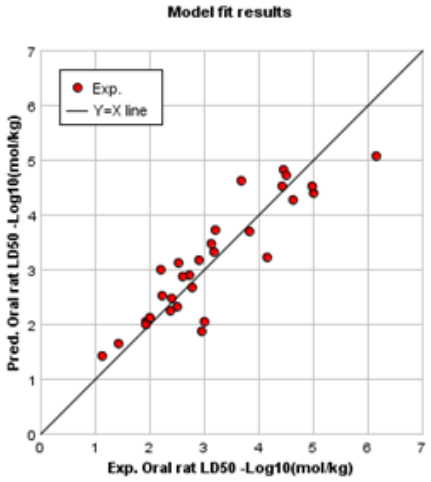


**Fig. 13. Statistical analysis and graph for oleuropein prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.638 |
| $q^2$ | 0.506 |
| #chemicals | 35 |
| Model | FDA Model |

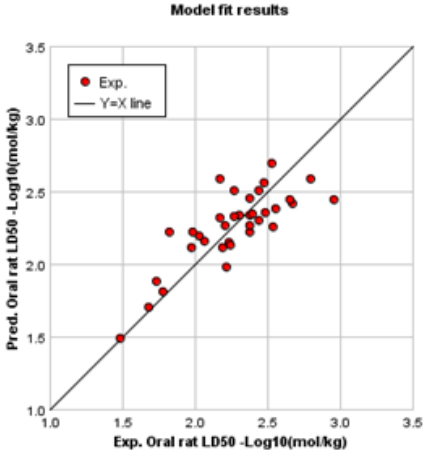


**Fig. 14. Statistical analysis and graph for thymol prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.803 |
| $q^2$ | 0.683 |
| #chemicals | 30 |
| Model | FDA Model |

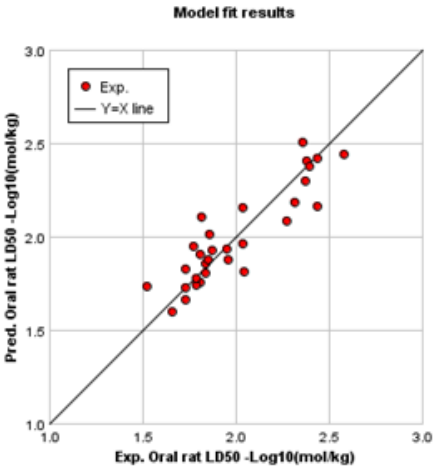


**Fig. 15. Statistical analysis and graph for eugenol prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.841 |
| $q^2$ | 0.767 |
| #chemicals | 30 |
| Model | FDA Model |

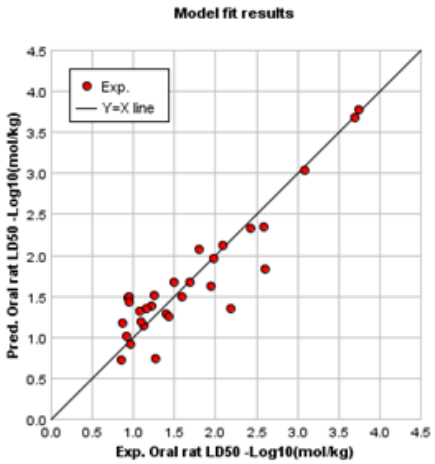


**Fig. 16. Statistical analysis and graph for ascorbic acid prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.906 |
| $q^2$ | 0.542 |
| #chemicals | 30 |
| Model | FDA Model |

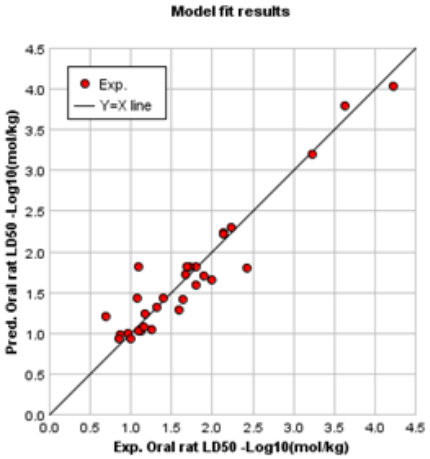


**Fig. 17. Statistical analysis and graph for tartaric acid prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.829 |
| $q^2$ | 0.699 |
| #chemicals | 29 |
| Model | FDA Model |

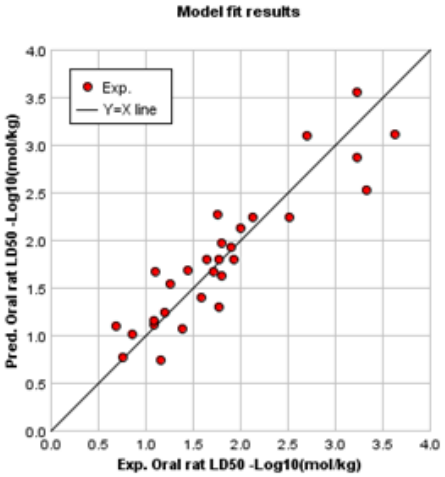


**Fig. 18. Statistical analysis and graph for malic acid prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.842 |
| $q^2$ | 0.717 |
| #chemicals | 30 |
| Model | FDA Model |

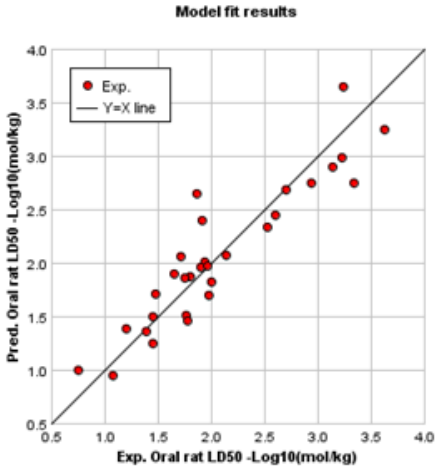


**Fig. 19. Statistical analysis and graph for fumaric acid prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.964 |
| $q^2$ | 0.948 |
| #chemicals | 30 |
| Model | FDA Model |

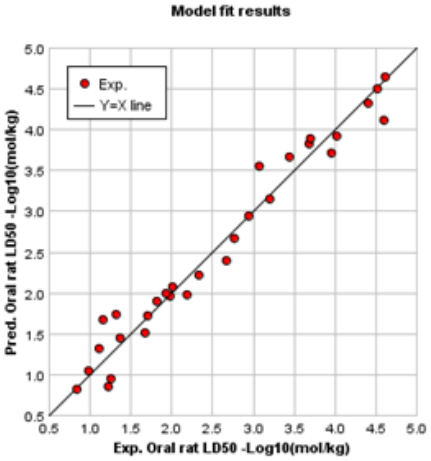


**Fig. 20. Statistical analysis and graph for tocopherol acetate prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.715 |
| $q^2$ | 0.536 |
| #chemicals | 35 |
| Model | FDA Model |

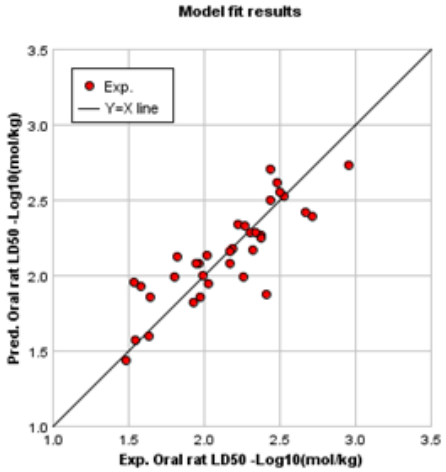


**Fig. 21. Statistical analysis and graph for carvacrol prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.764 |
| $q^2$ | 0.661 |
| #chemicals | 54 |
| Model | FDA Model |

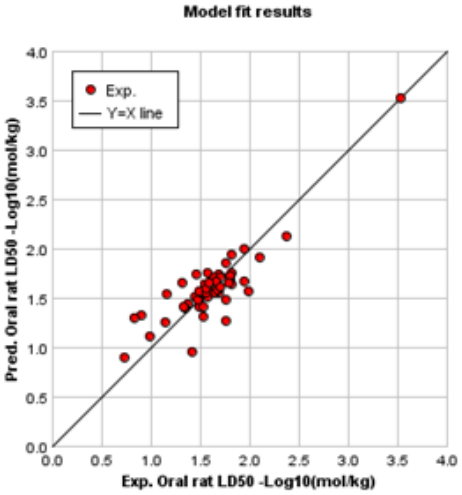


**Fig. 22. Statistical analysis and graph for citral prediction**

| Parameter | Value |
|---|---|
| Endpoint | Oral rat $LD_{50}$ |
| $r^2$ | 0.829 |
| $q^2$ | 0.714 |
| #chemicals | 30 |
| Model | FDA Model |

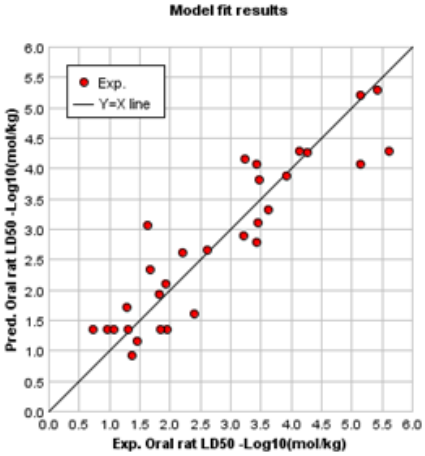


**Fig. 23. Statistical analysis and graph for allin prediction**

## DISCUSSION

The preservation of raw and processed foods always requires the chemical compounds known as preservatives, which protect the foods from bacteria and fungi (Soeda et al., 1966; Close and Nielsen, 1976). The preservatives are also very important to keeping food safe during usage and storage (Faruque, 2012). The present prediction results by using QSAR modeling software indicated that artificial preservatives viz. formaldehyde, and propionic acid and also benzoic acid were predicted lowest $LD_{50}$ value when compared to natural preservatives except thymol, fumaric acid and carvacrol (Table – 1). Moreover, the acute toxicity prediction with special reference to $LD_{50}$ value for both artificial and natural preservatives exposed orally in rat clearly revealed that natural preservatives have higher the $LD_{50}$ value compared to synthetic preservatives. It was well known by many researchers that food preservatives are safer when the chemicals are in natural origin as bioactive compound (Ou and Kwok, 2004; Narasimhan and Dhake, 2006; Chanwitheesuk et al., 2007; Pérez-Díaz and McFeeters, 2010; Mahiwal et al., 2012; Regnier et al., 2012; Belda-Galbis et al., 2013; Mohanka and Priyanka, 2014)

It was documented that artificial food preservatives such as sodium benzoate and sodium nitrite with a high and mid dose of nitrite compared to benzoate showed mortality in offspring of rat (Shuval and Gruener, 1972; Vorhees et al., 1984) while benzoic acid revealed acute toxicity with clinical symptoms in rats (Bio-Fax, 1973). It was reported few works on QSAR modeling of individual compound used as preservatives but the present findings were elaborative

study on acute toxicity prediction in rat after oral exposure of artificial and natural preservatives by using T.E.S.T. QSAR modeling software.

QSAR technique can be beneficial for discovering the relationship between the chemical molecular structures and their acute toxicities. It was known that the T.E.S.T. software estimates the predicted rat oral $LD_{50}$ values by calculating several 2D molecular descriptors (USEPA, 2012). These molecular descriptors have used to detect toxicity prediction in mammals by QSAR modeling (Gombar and Jain, 1987; Gombar and Enslein, 1990; Hall et al., 1991; Ruiz et al., 2012). Linear regression analysis is widely used as a final statistical method at the end of QSAR study (Xu, 2004; Li et al., 2010**)**.

In this present study, the rat oral $LD_{50}$ predicted values were obtained for QSAR modeling by using T.E.S.T. software. It was reported that T.E.S.T. software has better performance than other softwares like ADMET and TOPKAT for the prediction of sulfur mustard and its breakdown products on mammal (Ruiz et al., 2012). Previously worked on the acute toxicity prediction of fluroqunilone antibiotics in rat with T.E.S.T. software also predicted well with exact $LD_{50}$ value as per $R^2$ value of individual compound (Talapatra et al., 2015). According to studies by Canadian Center for Occupational Health & Safety (2012) and Ruiz et al. (2012), the toxicity ranges were determined as super toxic (<5 mg/kg), extremely toxic (5–50 mg/kg), very toxic (50–500 mg/kg), moderately toxic (500–5,000 mg/kg), slightly toxic (5,000–15,000 mg/kg) and practically non-toxic (>15,000 mg/kg) in the previous study of chemicals. The food preservatives were selected in the present study as per usage (Health Canada, 2012) but formaldehyde is non-permitted food preservatives (Janny, 2010). The present predicted acute toxicity results with special reference to $LD_{50}$ values of artificial and natural preservatives were showed that artificial preservatives viz. formaldehyde, and propionic acid and also benzoic acid were predicted lowest $LD_{50}$ value when compared to natural preservatives except thymol, fumaric acid and carvacrol. It is suggested natural preservatives might be used after conducting bioassay to correlate the present toxicity data from raw and processed food management perspective.

## CONCLUSION

The acute toxicity with special reference to $LD_{50}$ values in rat after oral exposure for 16 artificial and natural preservatives. Among 16 artificial preservatives, only 8 compounds were predicted and 15 compounds were predicted for artificial and natural compounds respectively. The results suggested that predicted acute toxicity of 3 artificial preservatives viz. formaldehyde, and propionic acid (>50 and <500 mg/kg) as very toxic and also benzoic acid (>500 and <5000 mg/kg) as moderately toxic were predicted lowest $LD_{50}$ value when compared to natural preservatives were within range of >500 and <5000 mg/kg as moderately toxic. This software has a potent capability to predict rat oral $LD_{50}$ value with suitable inbuilt programming of QSAR modeling with 2D molecular descriptors and similar test chemicals by calculating test sets and training set (Ruiz et al., 2012; USEPA, 2012). Although the benzoic acid and its derivatives were reported moderately toxic in experimental study as well as QSAR modeling (WHO, 2000; Li et al., 2010). Furthermore, natural preservatives in food are safer than artificial chemicals (Regnier et al., 2012) and management practices are suggested in relation to innovation of new brands of natural preservatives can be used from plant origin (Pérez-Díaz and McFeeters, 2010; Mohanka and Priyanka, 2014). This present prediction work was based on only single QSAR modeling approach but should need further investigation by using other softwares.

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