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Optimization of Analytical parameters and application in pharmaceuticals removal of Paracetamol onto Activated Carbon for sustainable environment

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Abstract

Pharmaceutical wastes have recently emerged as a significant source of water pollution, causing water-borne illness and significant changes to the aquatic biological cycle. The presence of pharmaceutical residues in the aquatic environment is a known problem worldwide; paracetamol (Para) is widely used as an analgesic and antipyretic. Its high consumption implies a continuous discharge in aqueous environments through industrial and domestic wastewater that requires mitigation and remediation strategies. In the present study, the activated carbon used is characterized by (F-TIR), (BET) and (MEB) to determine the physicochemical characteristics. Response surface methodology (RSM) was employed for the removal of (Para) onto activated Carbon (AC). Moreover, the numerical desirability function approach was adopted to statistically validate the output of Box-Behnken Design (BBD) results and to estimate the best operational adsorption conditions. The experimental data obtained were analyzed by analysis of variance (ANOVA) and fitted to a Second Order polynomial equation using multiple regression analysis. The optimum conditions were found to be (Dose = 0.1125 g, pH = 7, and T = 35 °C). A confirmatory experiment was performed to evaluate the accuracy of the optimization procedure and maximum (Para) removal of 99.58 % was achieved under the optimized conditions. Several error analysis equations were used to measure the goodness of fit. The adsorption follows well the Langmuir equation, providing a better fit of the equilibrium adsorption data. Under optimized conditions, up to 136.28 mg/g (R^2 = 0.97) at 25 ^oC is removed from the solution.

Keywords: Paracetamol, Adsorption, Activated carbon, Mechanism, Box Behnken, Isotherm,

Introduction

In recent years, development of new and more sensitive methods of analysis has alerted about the presence of residues of drugs, pharmaceuticals, veterinary, personal care, food additives, pesticides and other contaminants in water. These emerging contaminants reach the environment through domestic and industrial wastewater, waste from treatment plants, hospital effluents, etc. Elimination of these pollutants has become one of the greatest environmental concerns because of the impact they have on human health and the harmful effects they generate on nature **[1]**. Because of the substantial and widespread usage of drugs for both human and animal health care, drug residues are now pervasive in the environment. During the wastewater treatment process, removing drug residues could not be done entirely, resulting in accumulation in the aquatic environment, potentially impacting biodiversity, ecosystem functioning, and public health. Pharmaceuticals are an important group of potential endocrine disrupters which have recently attracted much attention of the international scientific community. They are emerging environmental contaminants, extensively and increasingly being used in human and veterinary medicine. These compounds are designed to have a specific mode of action, and many are persistent in the body. They have been detected with low concentrations (ng/L to µg/L) in many countries in many environmental samples, for example sewage-treatment plant effluents, surface water, seawater, and groundwater **[2, 3]**.

Conventional wastewater treatments for pharmaceuticals are ineffective in eliminating and/or degrading most of these compounds. Therefore, residual quantities remain in the treated water, and have been found to accumulate in drinking water **[4, 5]**. Particularly, paracetamol is one of the pharmaceuticals of common use worldwide due to its effectiveness in the relief of pain and fever. Unfortunately, its presence in recycled water has already been detected **[6].** Many pharmaceuticals undergo transformations in the human body, resulting in release of significant amounts of a variety of metabolites into the aquatic environment. These metabolites can be further transformed during sewage treatment. Pharmaceutical substances may also be degraded by biotic and/or abiotic processes, for example hydrolysis and photolysis. The degradation by-products are also of concern, because they may have toxicity similar to or higher than the parent compounds **[7, 8].** Paracetamol (N-(4-hydroxyphenyl) acetamide), also known as acetaminophen, is one of the most widely used analgesic and antipyretic worldwide. Due to its high stability, solubility and hydrophilicity it has been detected in surface waters, wastewater and drinking water throughout the world. (Para), as one of the most common drug used for analgesic and antipyretic purposes to treat fever and relieve pain, was found to have much higher concentration in aquatic stream and thus need to be removed efficiently. In wastewater treatment plants, (Para) is only partially removed from polluted water, because conventional wastewater treatment techniques are not specifically designed for emerging contaminants. Therefore, the presence of bioactive molecules in water intended for human consumption generates long-term toxicological risks since the drug can accumulate in adipose tissue at concentrations capable of generating biological activity. It is for this reason that new research efforts are currently being made to find new and effective water treatment methods like electro coagulation **[9, 10]**, flocculation **[11]**, adsorption **[12-18]**, ozonation **[19]**, membrane filtration **[20]**, and photo degradation **[21-23]** despite of large number of techniques available for the treatment of dye effluents. Among these, the batch adsorption process has been considered a superior physical technique for the removal of dyes from the industrial effluents. This technique is simple, easy to run, less time consuming, and the most effective process, except for the problem associated with the disposal of used biosorbents. Adsorption on porous solids is a very promising solution for removing organic and inorganic contaminants **[24]**. Activated carbons are among the most widely used adsorbents due to their versatility and favorable properties, such as their high specific surface area, porosity and specific chemical properties, which allow interaction with different chemical compounds. Indeed, the efficiency of adsorption on activated carbon strongly depends on the specific interactions between adsorbent and adsorbate, which in turn mainly depend on their chemical properties **[25-27]**. The present paper discusses response surface methodology (RSM) as an efficient tactic for predictive model and optimization of the whole experimental methods in the adsorption of paracetamol, however, research that optimizes the parameters based on the various parameters is lacking. It is important as it is difficult to observe the effects of several parameters on responses as it requires many extra experiments. Traditionally, parametric studies keep one of the factors constant while changing the other; however, this is a tedious task with less accurate results. Response surface methodology (RSM) with BBD design **[28]** is a widely used mathematical optimization with desirability method (df) through simultaneous analysis of interactions of multiple parameters with minimum experimental testing **[29]**, a multivariate optimization tool works on modeling based on factorial techniques and the Analysis of Variance (ANOVA) is useful as they extend the tools for a more detailed modeling of the parametric effects. RSM can also be used for prediction of responses based on the parameters once the analysis is complete.

Materials and method

Reagents

The pollutant studied is an antibiotic called paracetamol whose characteristics, structural formula and synthesis are grouped in **(Table.1)** purchased from Sigma-Aldrich (St Louis, MO, USA) in analytical purity. Different concentrations of paracetamol solutions were prepared by diluting a stock solution in distilled water. The adsorbent used for the elimination of the (Para) is a commercial Granular activated carbon supplied by Dinâmica Química Contemporânea (Diadema, SP, Brazil). Before use, the adsorbent was washed with water to remove carbon powder and surface impurities, followed by drying at 100 °C for 48 h. The size fraction between 2.00 and 2.38 mm was selected for all adsorption tests.

Characterization of the activated carbon

The Fourier Transform Infrared spectroscopy was used to identify the characteristic functional groups of commercial clay. 20 mg of AC were mixed with 80 mg of dry KBr of spectroscopy quality and pressed under a pressure of 4500 psi to form thin disc. Then, the FTIR spectra were plotted with a Perkin Elmer 2000 infrared spectrometer in the range (4000-400 cm^{-1}) for 16 times to increase the signal to noise ratio [30].

The N_2 adsorption and desorption isotherms were performed using a Tri Star II 3020 Micrometrics instrument that was used to obtain the textural characterization of the CCP 600 and CCP 700 adsorbent. The adsorbent samples were firstly dried for 12 h at 120 °C in an internal oven of the apparatus, and then the surface analyzer was run at − 196 °C for obtaining the N_2 isotherms of adsorption and desorption. The pore size distribution was calculated by the DFT method using the nitrogen adsorption branch [31]. The surface areas were calculated using the BET method [32].

The textural surface of activated carbons was investigated by scanning electron microscopy (SEM) (Jeol, JSM-6610LV, Japan) [33].

Adsorption experiments

The batch equilibration method was followed for the optimization process according to the CCD matrix**.** For this a precise amount of adsorbent was mixed with 0.1L of (Para) solution. The mixture was stirred with a magnetic agitation at 150 rpm at fixed contact time (40 min). Then, the separation was carried out by centrifugation at 6000 rpm during 10 min and the (Para) concentrations retained in the biosorbent phase were analyzed by UV–Vis spectroscopy at λ_{max} = 243 nm. The experiments were carried out under variable conditions of solution pH, initial dye concentration, adsorbent mass and temperature. HCl and NaOH (1.0 mol/L) were used to adjust the solution pH. To eliminate any interference with the adsorbates, blank tests were performed alongside the biosorption experiments by replacing the (Para) solutions with water.

Adsorption process optimization by response surface methodology

RSM is a statistical and mathematical method that, as previously mentioned, is used to optimize processes by minimizing the number of runs while concurrently establishing a relationship between the variables and responses. The Design Expert 12 software (Stat-Ease, Inc., Minneapolis, MN) was used to design the experiment, tabulate the responses, and analyze the experimental results. Optimization for maximum removal of strontium, barium, binary solutions including strontium and barium was employed using a Box-Behnken Design (BBD).

The Box-Behnken design (BBD) stands out among the array of response surface methodology (RSM) techniques as a highly effective multivariate statistical approach for optimizing multiple factors in diverse processes. Its efficiency and minimal experimentation requirements have made it widely adopted. Notably, BBD surpasses other designs such as the 3-level factorial design, central composite design, and Doehlert design due to its rotability and the absence of extreme factor combinations at highest and lowest levels, enhancing its efficiency further. The BBD statistical experimental design and RSM were used to study the

effects of the four independent variables on the response function. It is useful for optimization to examine the optimal conditions to take into account the response to lower or higher end results of a particular process **[34].** In this study, the most significant variables of (Para) adsorption were considered, pH (X_1), adsorbent dose (X_2), and temperature (X_3), in order to study their impact on color removal. The low, center and high levels of each variable are denoted by -1, 0 and 1, respectively **(Table.2)**. The provided quadratic polynomial equation represents the function of the response variable. Typically, the function of the response is influenced by the encoded variables:

$$Y = \mathbf{a_o} + \sum_{i=1}^{K} \mathbf{a_i x_i} + \sum_{i=1}^{k} \sum_{j=1}^{k} \mathbf{a_{ij} x_i x_j} + \sum_{i=1}^{k} \mathbf{a_{ii} x^2_i} \qquad \textbf{Eq.(1)}$$

Where Y is the predicted response which represents really the removal efficiency *R(%)* of (Para) adsorbed a_0 a constant coefficient, x_i and x_j variables.a_i, a_{ii} and a_{ij} are the interaction coefficients for linear, quadratic and second order terms, respectively.

The removal efficiency for each run was reported within ± 0.5 % precision, was calculated as the ratio of difference in initial and final (Para) concentration (C_0 - C_e) to the (Para) concentration (C_0):

$$\boldsymbol{R}(\%) = \frac{(\boldsymbol{C_0 - C_e}) \,.\, \mathbf{100}}{\boldsymbol{C_0}} \qquad \textbf{Eq.(2)}$$

C_e is the initial and equilibrium concentration of the Para (mg/L). The experimental matrix of CCD was proposed by Expert Design12 which was also used to determine the regression analysis of designed model and graphical analysis of each response. The total number of experiments calculated using the following equation:

$$\mathbf{N = K^2 + k + Cp} \qquad \textbf{Eq.(3)}$$

k =3, the number of independent variables, Cp =3, the number of experiment repeated at center points a total of experiments (N=15) were designed using the RSM method and optimized by a central composite design. Each experimental run was analyzed twice to avoid the effects of external factors, and the average values were considered. Analysis of variance (ANOVA) was used to analyze the statistical significance of each variable and adequacy of obtained regression equation. The experimental design matrix found according CCD along with response is given in **(Table. 3)**.

Modeling and Statistical Analysis

To anticipate the responses in coded values within the study's used ranges, individual linear, quadratic, cubic, and interactive mathematical empirical models were developed using the BBD approach. To determine the regression coefficients, the experimental data were fitted to the second order polynomial model. By computing *F* and *p* values of 0.05, the statistical significance level of each polynomial equation term was examined. To understand how the process factors affected the responses, three-dimensional surface plots were created. The determination coefficient (R^2) is an indicator for judging the quality of a linear, simple or multiple regressions. For a value between 0 and 1, it measures the adequacy between the model and the observed data.

ANOVA was performed to verify the statistical significance of the experimental design and establish interactions between independent variables and response effects **[35]**. It subdivides the total variation into two components, with variation associated with either the model or experimental error **[36]**. *F*- and *p*-values (prob >*F*, confidence interval = 95 %) for the model were obtained. The matching *F* and *p*-values of

the constructed models were used to evaluate them. Significant models correlated with higher *F* values and lower *p*-values. After optimization was concluded, the model equation was validated by comparing predicted and experimental values. ANOVA is a mathematical and statistical approach that subdivides the total data set alteration into ingredient parts concomitant with a defined source to test target hypotheses on the model parameters **[37]** to verify the statistical significance. The value of Fisher's *F* test, which is the ratio between the mean square of the model and the residual error, performs this comparison has been applied in this study **[38]**.

Results

Chemical Characterization

Surface functional groups within activated carbon give significant contribution toward its adsorption ability, primarily through providing selectivity to attract cation onto carbon surface **[39].** These functional groups are consisted mainly by acidic and basic groups which affect the surface charges and adsorption properties of activated carbon. Adsorption on activated carbon therefore not only relies upon its pore structure as the change of surface charges is also a crucial factor affecting the adsorption capacity. The FTIR spectrum can reveal the functional groups on activated carbon surface qualitatively based on the characteristic energy absorbed for each bond in certain groups, although some particular peaks may overlap. FTIR spectra of activated carbon were also determined by FTIR spectra as shown in **Figure.1.** The presence of C=O peaks around 1685 cm^{-1} can be identified, originated from bonding in carboxylic, lactone and another basic oxygen functional groups, i.e. chromene and pyrone structures. Peaks around 1025 cm^{-1} come from C–O bonding while the very broad peaks in wavenumber 3550–3200 cm^{-1} are recognized to be O–H functional groups for caboxyl and phenol. The presence of phenol is confirmed by the presence of peak around 1578 and 1610 cm^{-1} which was the absorption energy of benzene rings.

Textural Characterization

Nitrogen sorption isotherms for activated carbon is depicted in **Figure.2**, reveals different structures for activated carbon. The figure shows that the nitrogen sorption and desorption curves are practically confused and moreover a rapid adsorption of nitrogen at low relative pressure (P/Po less than 0.4) this indicates that activated carbon is mainly made up of micro pores (pore size < 20 A°) **[40].**

The BET surface area of activated carbon determined on the basis of nitrogen sorption is 1092.951 m^2/g. The micrographs of the AC **(Figure.3)** reveal that the exterior surfaces with more or less homogeneous cavities (micro pores) of different sizes and shapes, the latter are responsible for the fixation of the (Para) molecules inside these pores.

Experimental design analysis by central composite design

The main objective of RSM is to improve the response surface generated by process parameters. RSM offers a methodology for elucidating the response variable through an expression derived from a combination of several independent variables (pH, adsorbent and Temperature). This approach proves beneficial when defining numerous independent input variables with real values using intricate mathematical equations becomes challenging or unfeasible, a scenario encountered across various fields. When the independent variables in the system display autonomy, the response function adopts a linear structure. The relationship between the percentage uptake of (Para) and the three significant factors were illustrated by a second-order polynomial shown below:

$R(\%) = +96.671 - 2.3285\ pH + 554.829\ Dose - 2.21752\ T - 0.22035\ pH^2 - 1608.979\ Dose^2 + 0.0477\ T^2 + 25.846\ pH*Dose + 0.0495\ pH*T - 7.75429\ Dose*\ T.$

All positive coefficients ai and aij have a positive impact contributing to the increase in the efficiency of elimination of (Para) by activated carbon. On the other hand, the negative coefficients have a negative impact which favors the reduction of the elimination efficiency.

Validation of this model was carried out using the desirability function where the most desirable experimental conditions generated by the expert design were achieved. **Table.3** brings together the results obtained for the comparison of experimental yields R_{exp} (%) and those calculated by the mathematical model R_{pred} (%) during the eliminations of (Para) on activated carbon **(figure.4a)**.

To confirm the correlation of the results, a plot of the R_{exp}= f (R_{pred}) **Figure.4b** curve is carried out, and the linearity of the graph indicates that the models are in perfect correlation (R^2= 0.96). The responses were analyzed and the results of analysis of variance, and RSM were analyzed by Design Expert 12 for adsorption study. An ANOVA **(Table. 4)** was generated based on the experimental results according to the experimental conditions designed by RSM. In order to determine whether the effect of a coefficient is statistically significant, we compare the *p*-value with the alpha confidence level (generally taken as 0.05): if *p*-value < 0.05, the effect is significant; if greater (> 0.05), the effect is insignificant. In this case X_2 (Dose), X_3 (Temperature), X_1X_3 (pH, Dose), X_2X_3 (Dose, Temperature), X_2^2 (Dose, Dose) are significant model terms. X_1 (pH), X_1^2 (pH, pH), X_1X_3 (pH, Temperature) and X_3^2 (temperature, Temperature) p-Values greater than 0.06 indicate the terms are not significant.

The Lack of Fit *F*-value of 288.83 implies the Lack of Fit is significant. There is only a 0.35% chance that a Lack of Fit *F*-value this large could occur due to noise. Significant lack of fit is bad - we want the model to fit. The simplified second-order polynomial shown below:

$R\ (\%) = +96.671 + 554.829\ Dose - 2.21752\ T - 1608.979\ Dose^2 + 25.846\ pH*Dose - 7.75429\ Dose*\ T$

The predicted R^2 of 0.2725 is not as close to the Adjusted R^2 of 0.8724 as one might normally expect; i.e. the difference is more than 0.2. This may indicate a large block effect or a possible problem with your model and/or data. Things to consider are model reduction, response transformation, outliers, etc.

All empirical models should be tested by doing confirmation runs. Adequation precision measures the signal to noise ratio, a ratio greater than 4 is desirable. Your ratio of 12.079 indicates an adequate signal. This model can be used to navigate the design space. The coefficient estimate represents the expected change in response per unit change in factor value when all remaining factors are held constant. The intercept in an orthogonal design is the overall average response of all the runs. The coefficients are adjustments around that average based on the factor settings.

Discussion

Optimization by RSM and with desirability function

Traditionally, parametric studies keep one of the factors constant while changing the other, however, this is a tedious task with less accurate results. Response surface methodology (RSM), a multivariate optimization tool works on modeling based on factorial techniques and the Analysis of Variance (ANOVA) is useful as they extend the tools for a more detailed modeling of the parametric effects. RSM can also be used for prediction of responses based on the parameters once the analysis is complete. The Design Expert 12

provide a graphical route to study the model terms interactions by 2D contours and 3D plots**,** suitable to study the factors of binary interactions.

The 2D contour plots of the second-order polynomial equation within two independent variables (pH and temperature, adsorbent dose pH, pH and adsorbent dose temperature for Para, while all others are maintained at fixed values delivers the information on their connections and relationships; it can also include the main factor and the interaction impacts of two independent factors **[41]**. Examining the contours curves**,** of the binary variables (**Figure.5)** helps delineate the following optimal conditions to achieve maximum Para removal at (pH = 7, T= 35 °C; and adsorbent dose = 0.115 g/L).

The response surface plots Effect of interactive variables (*plots of surface 3D*) of the second-order polynomial equation with two variables were kept constant and the other two varying within the determined experimental ranges are given in **Figure.6** witch present the response surface plots of the effect of (Dose-Temperature), and (pH- Adsorbent dose and (pH and temperature) respectively on the adsorption of (Para) onto AC respectively the optimal conditions to achieve maximum Para removal at (pH = 7, T= 35 °C; and adsorbent dose = 0.115 g/L).

Optimization using the desirability function by using numerical optimization, a desirable value for each input factor and response can be selected. Therein, the possible input optimizations that can be selected include: the range, maximum, minimum, target, none (for responses) and set so as to establish an optimized output value for a given set of conditions. In this study, the input variables were given specific values, whereas the response was designed to achieve a maximum. Using these conditions, the maximum achieved fluoride removal efficiency was 90.83% **(Figure.7)** at an initial pH of 6.7, adsorbent dose of 0.1125 g, and temperature of 42 ^{o}C. The confirmatory experiment showed a (Para) removal efficiency of 95.78% under optimal conditions compared with the (Para) removal percent of 98.24% obtained by the model. This indicates the suitability and accuracy of the model to simultaneously know the optimal parameters (pH = 5.03, T= 42 °C; and adsorbent dose = 0.125 g/L with R (%) = 89.99) of the input variables that determine the optimal performance levels for one or more responses and proceeds in two steps:

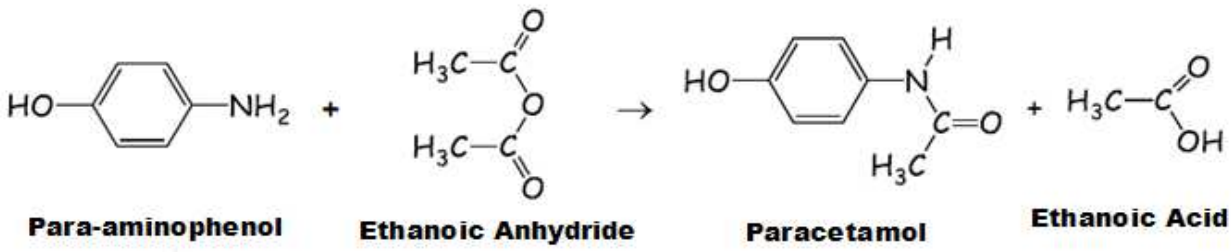
i) Find the levels of the independent variables that simultaneously produce the most desirable, predicted responses on the dependent variables.

ii) Maximize overall desirability with respect to controllable factors, the desirability function approach was initially introduced by Harrington **[42]**.

Perturbation plots Additionally, **figure 8** displays perturbation curves for all the responses based on different parameter conditions in this study A (pH), B (Temperature) and C (Dose). The slope of each curve indicates the sensitivity of the responses to the respective factors. Notably, factors B (temperature) and C (dose) exhibit the highest slopes, indicating that they have the most significant impact on all the responses.

Mechanism of synthesis of paracetamol

Paracetamol does not include a stereogenic center and has no stereoisomers. The synthesis does not need to be stereo controlled and is simpler than asymmetric syntheses of other pharmaceutical substances. (Para) was first synthesized in 1878 by Harmon Northrop Morse. The first step is the reduction of (Para) nitrophenol to para-aminophenol in the presence of tin in glacial acetic acid. The para-aminophenol obtained is then acylated by acetic acid to obtain (Para) **[43]**. Vignolo simplified this synthesis by using para-aminophenol as a starting product. Only one acylation step is necessary to obtain the desired product, which shortens the synthesis. The synthesis of (Para) is illustrated by the following reaction:



Later, Friedlander modified the synthesis by acylation of para-aminophenol from paranitrophenol with acetic anhydride instead of acetic acid, which gave a better yield **[44]**.

$$C_4H_6O_3 + C_6H_7NO \rightarrow C_8H_9NO_2 + CH_3COOH.$$

Nowadays, there are different industrial synthesis methods, most using the acylation of para-aminophenol with acetic anhydride.

The infrared spectroscopy of (Para) is illustrated by (**Figure.9).** The band centered at 3200-3670 cm^{-1} is attributed to both O-H stretching vibration of alcohol and acidic groups; This molecule belongs to the functional class of amides. On the other hand, it does not belong to the functional class of alcohols, but to that of phenols due to the fixation of the hydroxyl group on an aromatic ring. The band at 3600 cm^{-1} corresponds to the O-H bond, that at 3400 cm^{-1} to the bond N-H, that at 3000 cm^{-1} to the C-H bonds are attributed to C-H symmetric and asymmetric stretching vibration modes **[45]**, that at 1750 cm^{-1} to the C=O bond and finally that at 1500 cm^{-1} bonds is attributed to C=C aromatic stretching vibration with a higher intensity. The peak 1349 cm^{-1}, attributed to C-N stretching for the spectrum. In the condensed phase, a very wide band of strong absorption centered around 3300 cm^{-1}, corresponding to hydrogen bonds involving both N-H bonds and O-H bonds between different molecules present in solution.

Adsorption isotherm models

Adsorption isotherms which describe how an adsorbate interacts with the adsorbent are critical in optimizing the adsorption. The amount of adsorbate per unit mass of adsorbent at equilibrium, q_e (mg/g) and the adsorbate equilibrium concentration, C_e (mg/L) allow plotting the adsorption isotherm, q_e versus C_e, (**Figure.10**) mathematical models can be used to describe and characterize the adsorption processes. The experimental data were fitted to four common isotherm models: Langmuir, Freundlich, Temkin and Elovich which describs the solid-liquid sorption of (Para) onto AC.

Langmuir model **[46]** postulates the occurrence of monolayer adsorption onto a fixed number of localized sites on an adsorbent surface. The model assumes that a given adsorbent surface is composed of sites equivalent in their enthalpies but with no further motion of the adsorbed molecules on the surface, and no interactions between the adsorbed molecules; the linear expression is given by**:**

$$\frac{1}{q_e} = \frac{1}{q_m} + \frac{1}{q_m.K_L.C_e} \qquad (6)$$

$$R_L = \frac{1}{(1+K_L C_0)} \qquad (7)$$

The type of isotherm is indicated by the R_L value: (R_L= 0): irreversible, (0 < R_L< 1): favourable, (R_L= 1): linear, (R_L>1): unfavourable.

Freundlich's model **[47]** is based on the formation of multilayer's of adsorbed species on a heterogeneous surface. The adsorbent surface site enthalpies have a logarithmic distribution, where the energy sites with

high affinity for the adsorbate are occupied first, followed by sites of lower energy. The sorption process is summed over all sites and the linear expression of the Freundlich model is given by:

$$\boldsymbol{ln\, q_e = ln\, K_F + \frac{1}{n} lnCe} \qquad \textbf{(8)}$$

K_F (L/g) and *n* are constants, related respectively to the capacity of adsorption and favorability of adsorption extracted from the plot lnq_e versus lnC_e. When *n* is between 2 and 10, favorable adsorption is expected, while *n* value less than unity indicates poor sorption characteristics.

Similar to Freundlich's model, Temkin's **[48]** postulates the heterogeneity of an adsorbent surface, whose distribution of adsorption energy is linear; the non-linear form is given by:

$$\boldsymbol{q_e = B_T lnC_e + B_T lnA} \qquad \textbf{(9)}$$

$$\boldsymbol{B_T = \frac{q_m.R.T}{\Delta Q}} \qquad \textbf{(10)}$$

$\Delta \mathrm{Q}(\mathrm{J/mol})$ is the adsorption energy change and $\mathrm{q_{max}}\ (\mathrm{mg/g})$ the maximum adsorption capacity. The adsorption data are analyzed according to the linear plot q_e versus lnC_e, enabling to calculate the constants A_T and B_T.

Elovich model **[49]** assumes that the number of adsorption sites augments exponentially with the adsorption, thus implying a multilayer adsorption:

$$\boldsymbol{ln\frac{q_e}{C_e} = ln(K_E.q_m) - \frac{q_e}{q_m}} \qquad \textbf{(11)}$$

Where K_E (L/mg) is a constant, q_{max} (mg/g) the maximum adsorption capacity, q_e (mg/g) the adsorption capacity at equilibrium and C_e (g/L) the concentration of the adsorbate at equilibrium. Both the constants K_E and q_e are calculated from the plot of ln (q_e/C_e) versus q_e.

To investigate the Para uptake, the adsorption isotherms were applied to evaluate the accumulation amount of adsobate onto the adsorbent surface and the type of interaction Para-adsorbent. The graphic representation of the linearized forms of the four isotherms models enabled us to calculate the constants of the different models, grouped in **Table.5**. Fitness evaluation of experimental equilibrium data by conventional models, based on the coefficient R^2 as a criterion, shows the applicability of Langmuir and Temkin models for the interpretation of data with maximum adsorption capacity q_{max} (136.28 mg/g ,R^2 = 0.97, at 25 °C). The Langmuir model was best suited to fit the experimental data. Noted that R_L indicates the type of isotherm: Irreversible (R_L= 0), Favourable (0<R_L<1), Linear (R_L=1) or unfavourable (R_L> 1). In our case, the R_L values are smaller than 1, thus confirming that adsorption is well described by the Langmuir isotherm which suggests one of the following three main hypotheses:

a) The adsorption sites have identical adsorption energy.
b) The adsorbate occupies only one site on the surface
c) The adsorption is mostly confined to the adsorbent surface.

Performance and regeneration of the AC

In order to reveal the reference of the AC for the removal (Para), a comparative study was undertaken with the other adsorbents in the literature where the maximum Langmuir adsorption capacities q_{max} of the different adsorbents is used as criterion **(Table.6)**. It is seen that and adsorption in the present study are well classified with q_{max} capacity of 136.28 mg/g. AC is an interesting adsorbent for pollutants due to its isoelectric point p*H(pzc*).

The reusability of the adsorbent for further studies is a key consideration as it promotes cost-effectiveness, environmental friendliness and the circular economy **[50].** The selection of the solvent as the pollutant is essential for the recovery of adsorbates as well as free active sites for the subsequent adsorption process. Several methods exist for regeneration such as electrochemical, microbiological, thermal and chemical processes. We opted for the chemical method because of its low cost; indeed, the regeneration and reuse of adsorbents for other cycles is economically important.

The desorption of (Para) from AC was evaluated using three different solvents: H_2O, NaOH and HCl**.** The highest desorption was achieved in HCl solution with a rate of 90.56 % against 78.24 % (NaOH) and 45.23 % (H_2O). This result suggests that AC was suitable for 3 cycles (R_1=90.56 %, R_2 = 78.26 %, R_3 = 45.25%) However, there is a gradual decrease in adsorption from cycle 1 to cycle 3, which could be attributed to the alteration of the surface structure of the adsorbent, thus leading to the blocking of several adsorption sites.

Conclusion

The removal of pollutant contaminants from wastewater is a critical environmental concern especially concerning contaminants like heavy metals dyes and pharmaceutical effluents, predominantly originating from industries, which pose significant risks to human health and ecosystems due to their toxicity. Activated carbon has emerged as a promising adsorbent for the efficient removal of these pollutants; however, optimizing the adsorption processes is essential to maximize efficiency. In this study, the statistical methodology, Box–Behnken Response Surface design is demonstrated to be effective and reliable in finding the optimal conditions for the adsorption of paracetamol onto activated carbon. The results showed that, the adsorption conditions have significant effects on the removal of paracetamol. The response surface plots were used for estimating the interactive effect of four independent variables (pH, temperature and adsorbent dose) on the response (percent of praracetamol adsorption). The second order mathematical model was developed by regression analysis of the experimental data obtained from 15 batch runs. The experimental data obtained were analyzed by analysis of variance (ANOVA) and fitted to a second-order polynomial equation using multiple regression analysis. Numerical optimization applying desirability function was used to identify the optimum conditions for maximum removal of (Para). The optimum conditions were found to be (Dose = 0.1125 g, pH = 7, and T = 35 °C). A confirmatory experiment was performed to evaluate the accuracy of the optimization procedure and maximum (Para) removal of 99.58 % was achieved under the optimized conditions. Several error analysis equations were used to measure the goodness of fit. The adsorption follows well the Langmuir equation, providing a better fit of the equilibrium adsorption data. Under optimized conditions, up to 136.28 mg/g (R^2 = 0.97) at 25 ^oC is removed from the solution. This study demonstrated that the AC has relatively high adsorption capacity compared to some other adsorbents reported in the literature and the combination tests of this adsorbent with semiconductors for studies of the photo degradation of paracetamol constitute the logical continuation of this work.

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Authors Contributions

M. ABBAS: Conceptualization, Methodology, Visualization,
M. ABBAS, T AKSIL: M. TRARI, Investigation, Validation, Data curation, Writing – original draft, review & editing.

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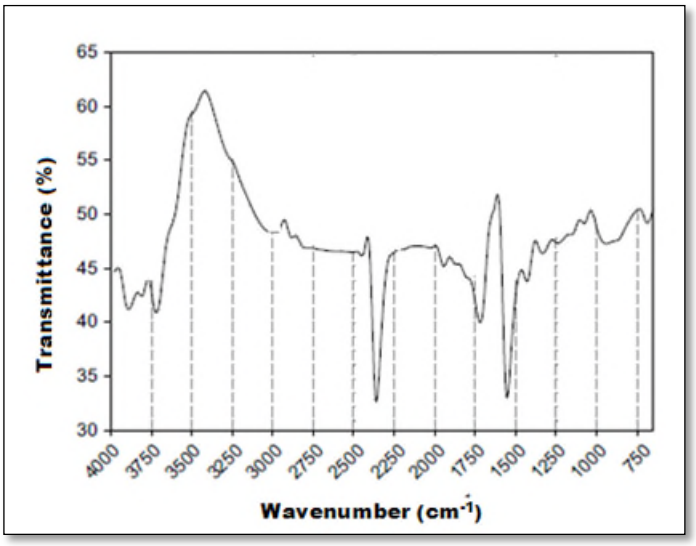


Figure.1: *FTIR spectra for activated carbon.*

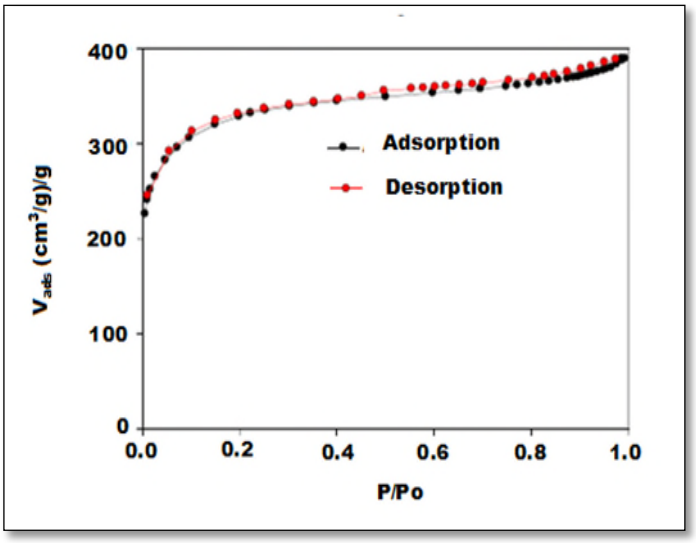


Figure.2: *Nitrogen sorption and desorption isotherms for activated carbon*

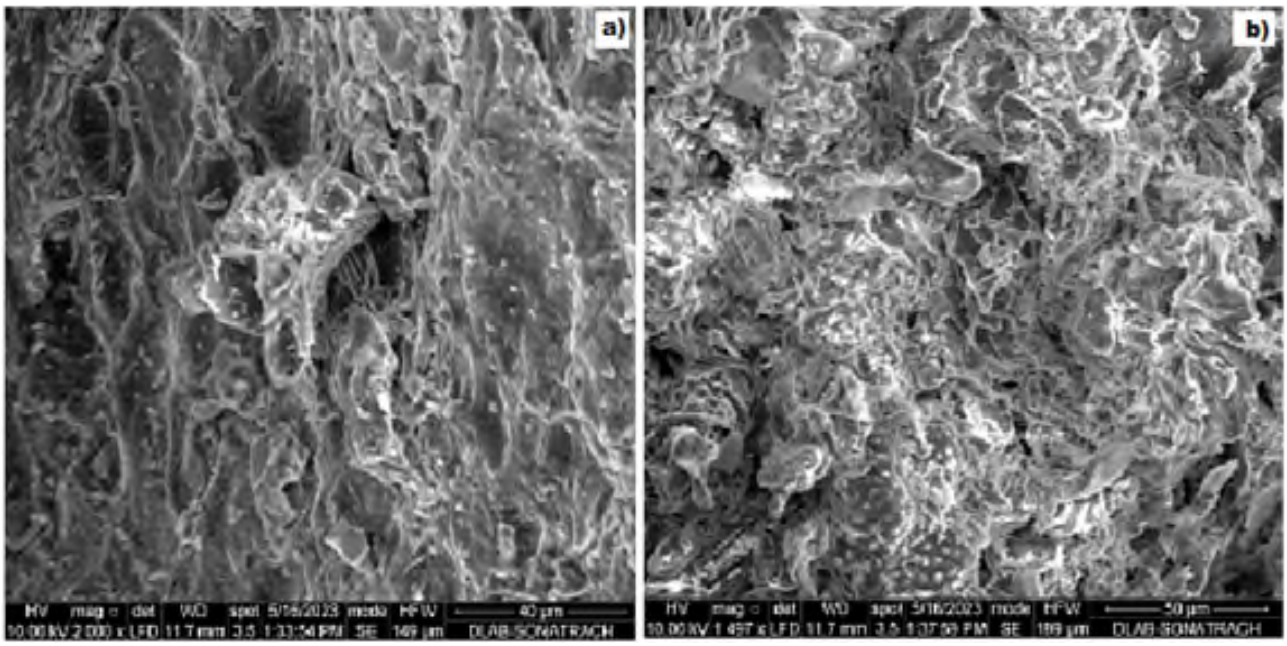


Figure.3: *Nitrogen sorption and desorption isotherms for activated carbon*

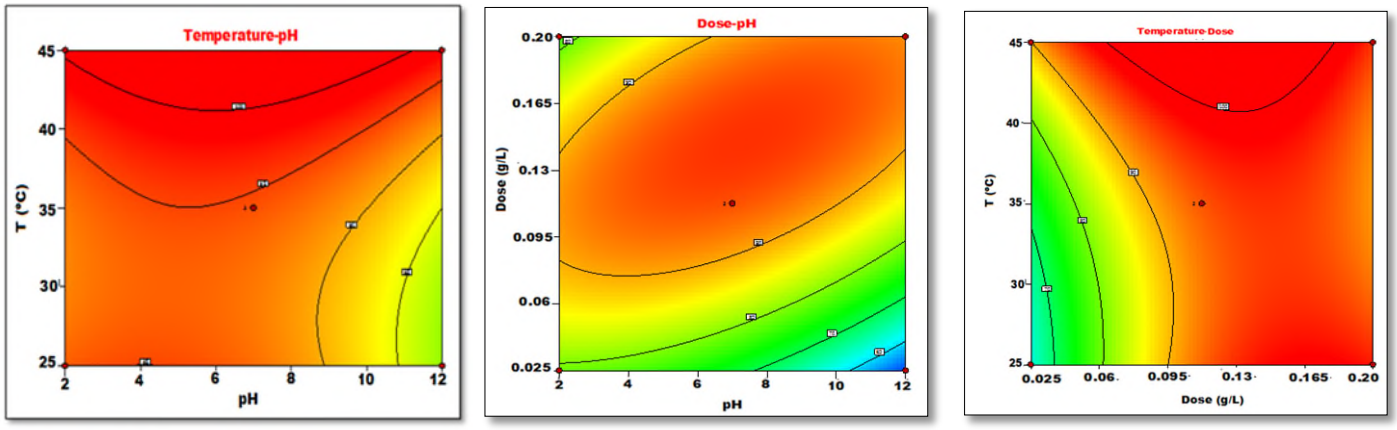


Figure.4: *Contours plots (pH =7, Dose = 0.1125, T = 35 °C)*

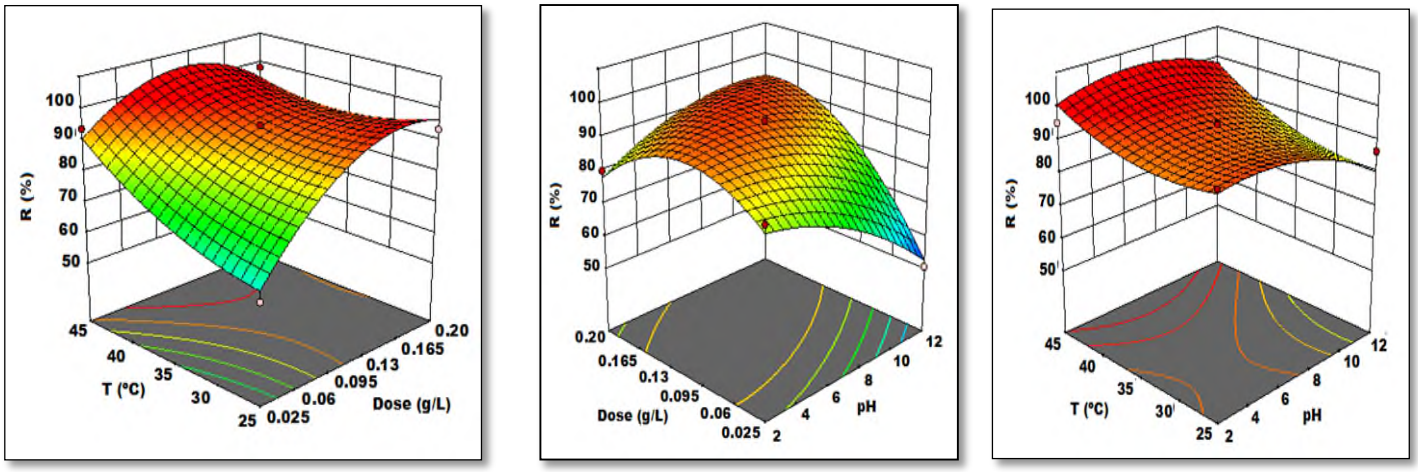


Figure.5: *The three - dimensional response surface plots for (Para) removal onto AC (pH = 7, Dose = 0.1125, T = 35 °C)*

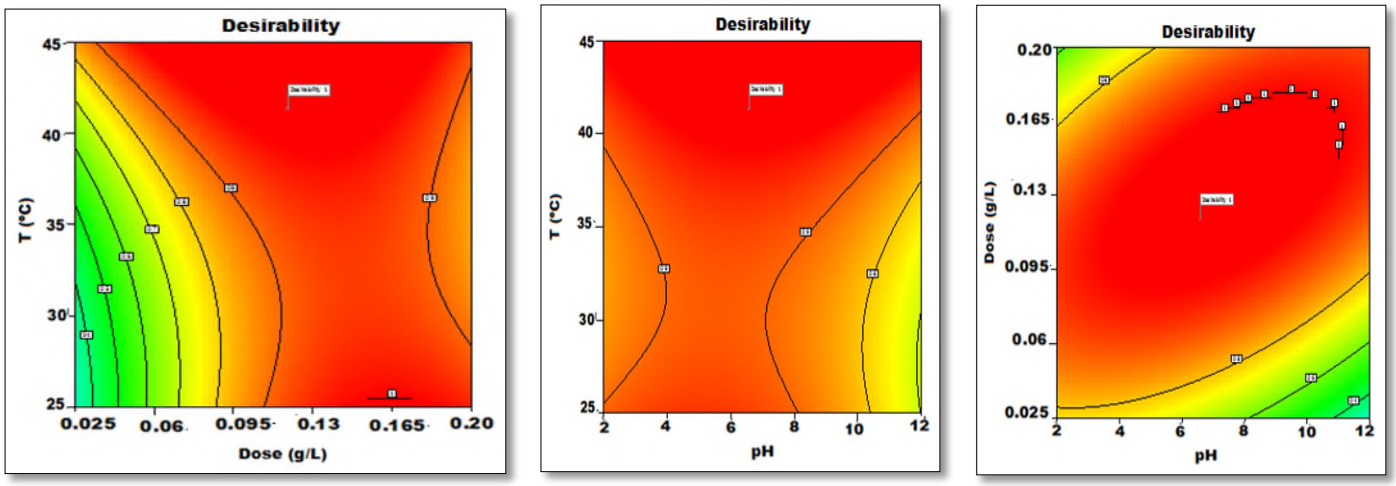


Figure.6: *Desirability Plots: (pH = 6.7, Dose = 0.1125 , T = 42 °C)*

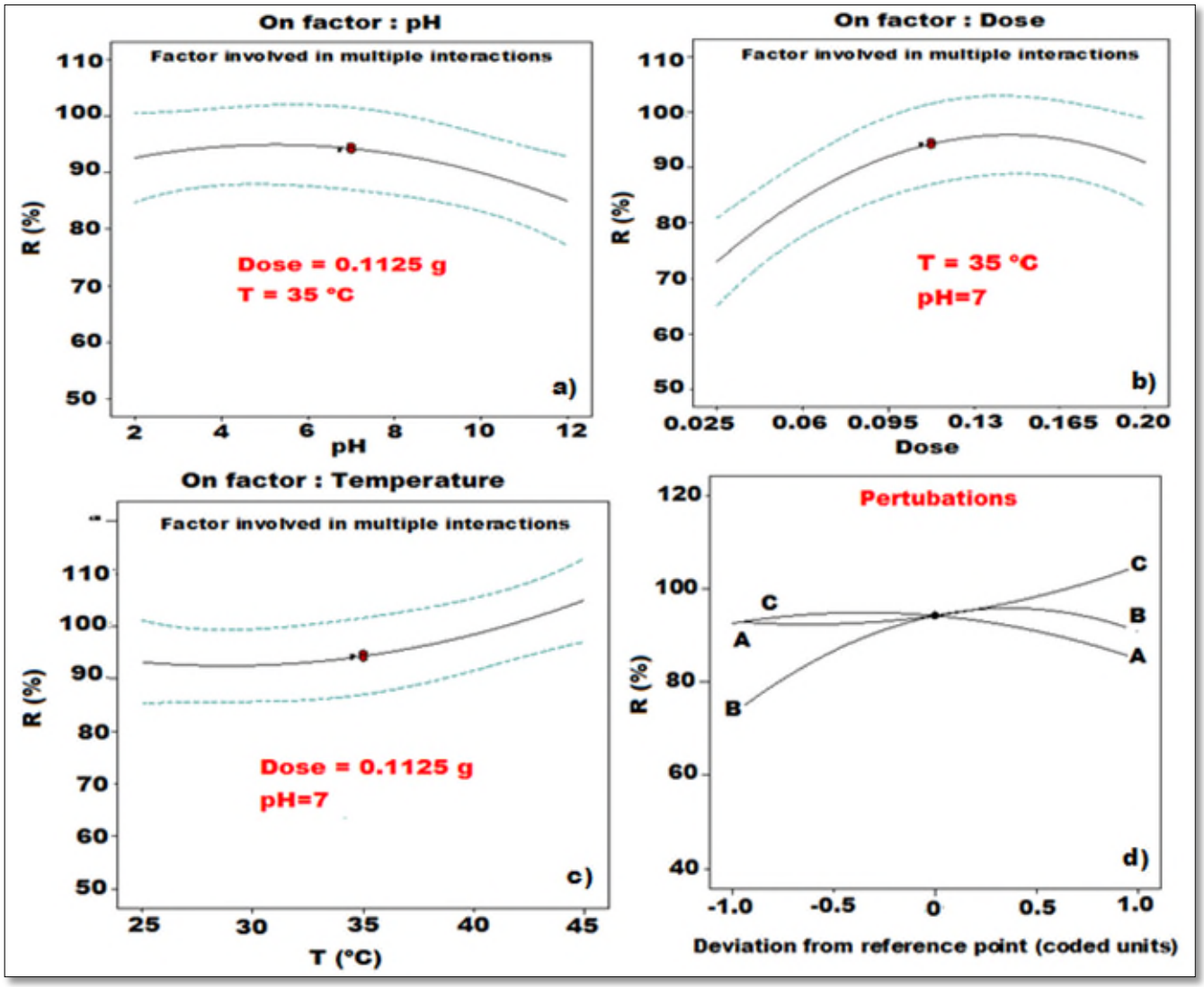


Figure.7: ***Perturbation plots: a)*** *pH* ***b)*** *Adsorbent dosage* ***c)*** *Temperature* ***d)*** *pH-Dose-Temperature*

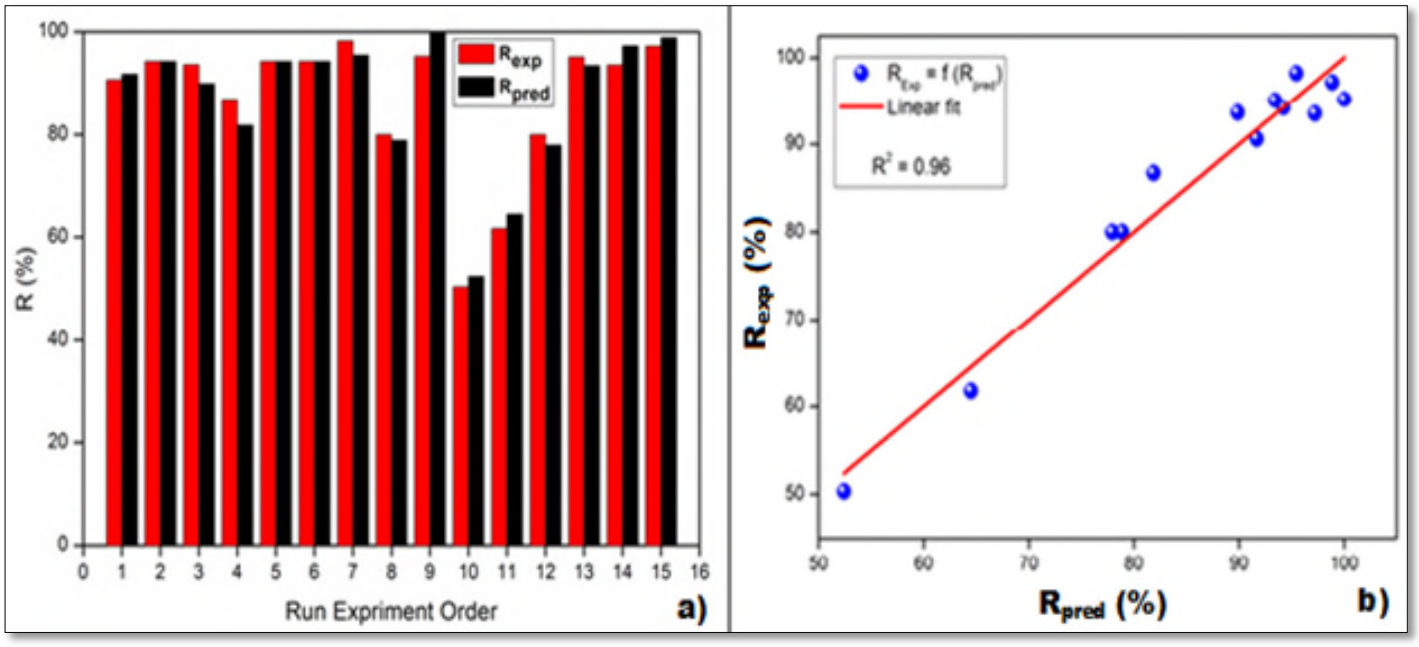


Figure.8: ***ANOVA results, Residuals vs. predicted and Removal comparison***

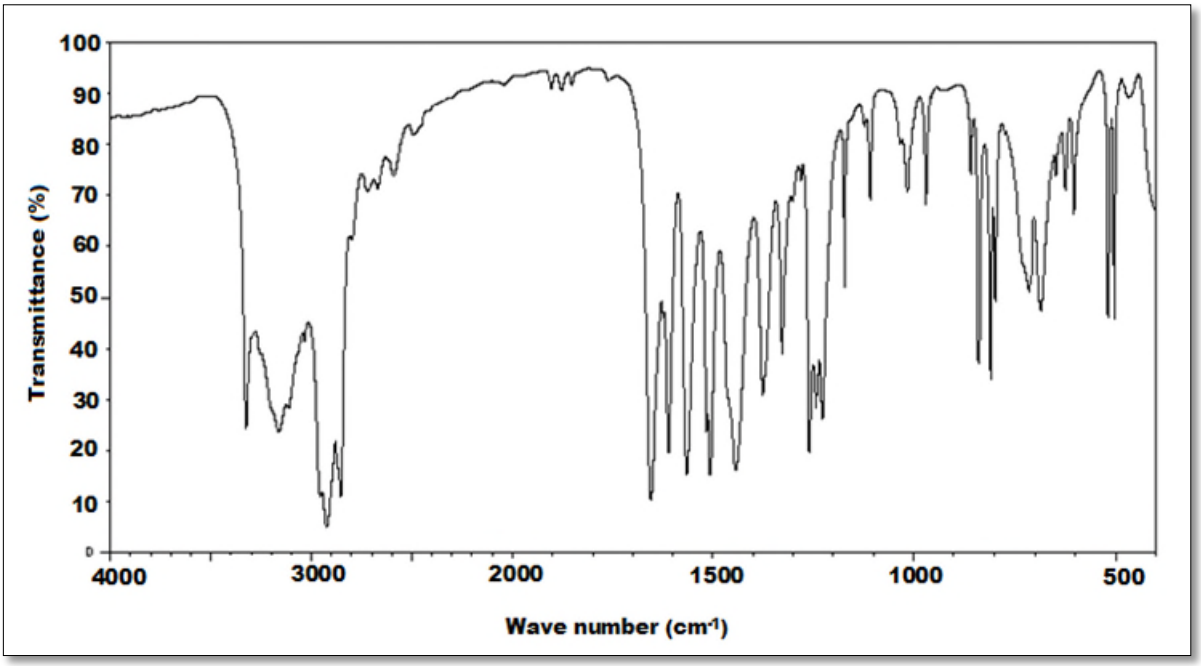


Figure.9: ***FTIR spectra for Paracetamol***

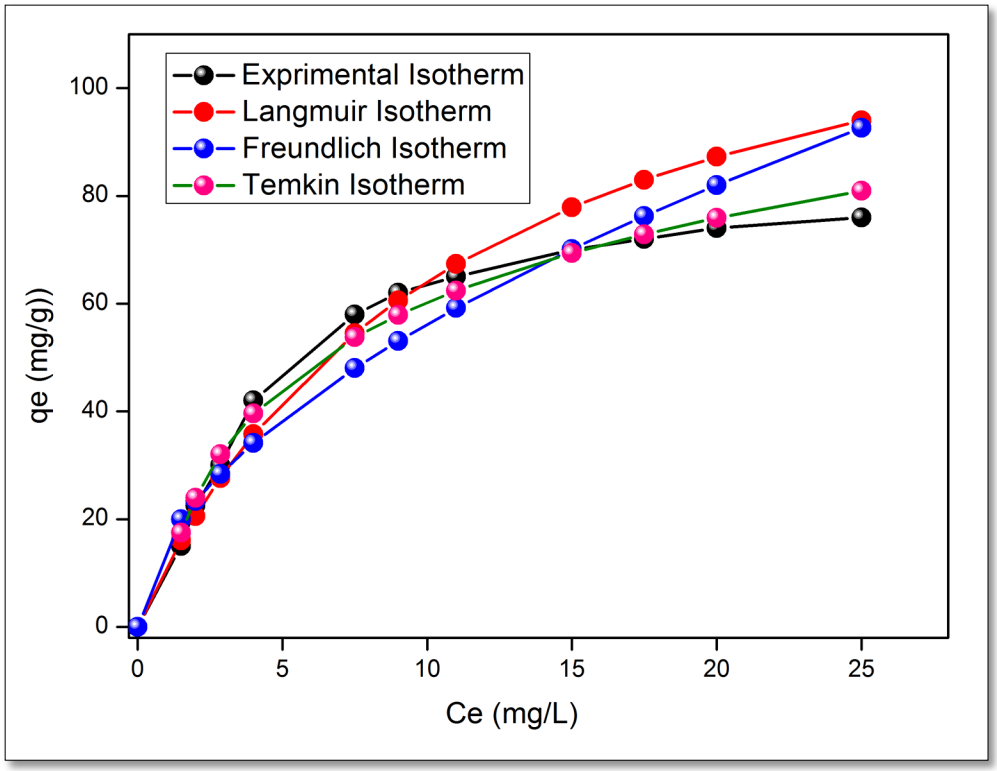


Figure 10: ***Isotherms in the optimum condition***

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