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Detoxification of acetaminophen overdose using formulated carbo tablets

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ABSTRACT

Acetaminophen overdose is one of severe global health challenges. In this study, adsorption technique was used to reduce acetaminophen overdose. Carbo tablets derived by wet granulation technique, coded as formulated carbo tablet (FCT) and alginated formulated carbo tablets (FCT-Alg), were characterized using the pharmaceutical drug procedures (hardness, disintegration time, tablet strength, friability) and instrumental techniques including, FTIR, SEM, and DSC analysis. DSC thermogram revealed that, the excipients were compatible with the active pharmaceutical ingredient (API). Batch adsorption experiments were carried out in the simulated gastric fluid (SGF) to monitor the role of some parametric factors (pH, concentration, carbo dosages, and PCM dosages). The tablet displayed favorable hardness and disintegration time (3.40 min). Optimum adsorption was observed at pH 1.2 for FCT in SGF (RE of 92.80%); FCT-Alg in SGF (RE of 99.17%). The results depicted that, the adsorption of the acetaminophen in SGF gave up to 99.65% removal efficiency, and compared with the commercial carbo tablet (CCT) with adsorption efficiency of 96.44%.

Graphical Abstract

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Introduction

Acetaminophen as an analgesic agent is the main cause of acute liver failure in both developing and the industrialized countries. Acetaminophen overdose can be managed by utilizing activated charcoal. The ease of administration and its relative safety when compared with other gastrointestinal decontamination methods makes it desirable for drug overdose management [1]. Large reductions in drug absorption occur soon after drug ingestion.

Acetaminophen poisoning

Acetaminophen poisoning has been reported in Nigeria in pediatric cases, led to deaths of 40 children, and in adults who used more than three brands of medications for pains containing acetaminophen. It caused liver damage except where immediate treatment is given via activated charcoal slurry or the acetyl cysteine antidote [2].

It was reported that, untreated acetaminophen overdose resulted in a lengthy and painful illness [2]. Signs and symptoms of acetaminophen toxicity may initially be absent or non-specific symptoms. The symptoms of overdose are including nausea, vomiting, sweating, and pain as acute liver failure starts [1]. People who take overdoses of acetaminophen do not fall asleep or lose consciousness; however, most people who attempt suicide with acetaminophen wrongly believe that they will be rendered unconscious by the drug [3]. The process of dying from an overdose takes from 3–5 days to 4–6 weeks [4]. Figure 1 is the chemical structure of acetaminophen.

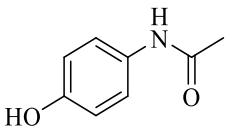


Figure 1. Acetaminophen [4].

Activated charcoal is a product of controlled pyrolysis of organic material activated by heating in an oxidizing gas at high temperature [5]. It is used as a nonspecific gastrointestinal (GI) decontaminant in poisoning, and it is often used even if the poison has specific antidote. For this reason, easily re-suspendable and efficacious preparation of AC should be available in the emergency rooms or nearby [2, 3]. The activated charcoal can be used to decrease the absorption of the acetaminophen if the person comes to the hospital soon after the overdose [1, 3]. Kidney failure is also a possible side effect [6].

Carbo tablet

Carbo tablet is used clinically to treat the intoxications caused by toxic chemicals taken orally, toxins generated in the gastrointestinal tract, and drug overdose [7]. In addition, it is useful to remove the waste products from the bloodstream. It can adsorb various chemicals, removing them from the body [8]. Carbo tablet is low in toxicity and price, and does not cause the emergence of drug-resistant strains of bacteria. Previously, it was demonstrated that Carbo tablet revealed a good potential to adsorb an endotoxin which was related to serious symptoms of food poisoning, and Carbo tablet with a size of 150-200 mesh showed a large capacity to adsorb an endotoxin [9].

Figure 2. Carbo Tablet and capsules [10].

A modified wet compression method using carboxymethylcellulose sodium (CMC-Na) solution as binder solution, croscarmellose sodium (CC-Na) can be used as a disintegration agent, medicinal carbon granules, and binder solution can be placed in the cylinder to form the tablet. The obtained tablets can be examined for hardness, disintegration rate, dissolution, controlled release, and adsorption profiles [6]. This research aimed at investigating the adsorption profile of the acetaminophen onto formulated and commercial carbo tablets. The objectives underlying this study include formulation of carbo tablet from commercial activate carbon, using pharmaceutical drug formulation procedures, characterization of the derived carbo tablets and investigation of sorption profile. The present study, however, simulated the gastric fluid (SGF) to create near stomach environment for acetaminophen dissolution and uptake.

Materials and methods

The materials used in this research were including the commercial medicinal carbo tablet, acetaminophen, hydrochloric acid, NaCl, distilled water, Alginic acid sodium salt, Talc powder, magnesium stearate, bentonite, and corn starch. All chemicals used for carbo tablet formulation were used without further purification. The dissolution media had the pH of 1.2 and 6.8 for the simulated gastric fluid (SGF) buffer, sodium chloride, and hydrochloric acid. All the solutions were prepared using distilled water. Scanning electron microscope equipped with energy dispersive X-ray spectroscopy (EDX, model S-3400N), Fourier-transform infrared spectroscopy (FT-IR, model Metler-Star/SW13.00), differential scanning calorimeter (DSC), and UV spectrophotometry (model 752N) were employed to evaluate the material

Sampling

Commercial carbo tablet (Merck KGaA, Darmstadt, Germany) was procured from Wino pharmaceutical, wadata, Makurdi, sodium alginate ($C_6H_7Na\ O_6$)n; Net. Wt: 500g; ES. No.0/HG31976-99, was supplied by Merck chemicals, India). Bentonite and starch were supplied by Joechem scientific co. ltd, Nsuka, Enugu state. Analytical grade acetaminophen (Merck A500); CAS Number 103-90-2, Mol. Wt: 151.16 g, Talc, and magnesium stearate were graciously donated by Mr. Agbo. of the formulation laboratory (pharmaceutical department) of ABU Zaria, Nigeria.

Sample preparation

The commercial granular activated carbon was pulverized using a mortar, pestle and blender. The powder mixture was prepared on volume basis containing 60% excipients and 40% drug compound. The powders were mixed in a high shear impeller mixer at a mixing time of 4 min. Homogeneity of the mixtures was then tested. The mixing time was extended gradually, in 2-min steps, the maximum being 8 min, if the desired homogeneity was not achieved earlier [6].

Acetaminophen stock (1000 ppm) was prepared. 1 g of pure sample (analytical grade) of acetaminophen was weighed, dissolved in a beaker containing small quantity of distilled de-ionized water and transferred into a 1000 cm^3 volumetric flask and make to mark with distilled water. The content was appropriately diluted and required aliquot was taken for preparation of calibration curve, from1000 ppm stock solution and the process was used for SGF used as dissolution medium [11]. UV absorption maximum was assessed using scanning the 10 ppm acetaminophen solution and SGF between 200-400 nm region of the UV-visible spectrophotometer. An absorption maximum of 264 nm was obtained. The standard solutions for the drug with the concentration of 5, 10, 15, 20, 25, and 30 ppm was prepared with SGF, pH of 1.2 from the stock solution. The absorbance of solutions of pure acetaminophen drug was measured at 264 λmax and a calibration curve was plotted for linearity and regression equation [4].

Simulated gastric fluid without enzymes (SGF)

The SGF was prepared in accordance with the USP 30 standard method by dissolving 2 g NaCl in 7 mL of concentrated HCl and filled up to 1 L with distilled water free of CO_2 and simultaneously adjusting the pH of the solution to 1.2. Acetaminophen was added to the SGF solution to reach a concentration of 2500 mg/L. The calibration curve of acetaminophen in SGF was performed using a UV-vis spectrophotometer (model 1800, USA). The optical density of all samples was determined with maximum absorbance scanned at $\lambda_{max} = 264$ nm in the zone of Lambert Beer transmittance [3].

Formulation of carbo tablets (wet granule compression)

The tablet was formulated (Table 1) at the formulation laboratory of the department of pharmaceutical science, Ahmadu Bello University, Zaria Nigeria, using the Tableting machine (model ErwekaAr 400, Germany), according to the United States Pharmacopoeia (USP 30) standard method. The wet granule was dried overnight. The dried granule (500 mg) was placed in a cylinder (500 mg cavity inner diameter) and tableted. The tablet was preserved in a glass bottle at room temperature, and used 24 h after the production [6, 12, 13]

Table 1. Composition of Formulations of Carbo Tablet Derived Based on USP 30 Method.

Excipients	FCT (mg)	FCT-Alginate (mg)
Charcoal (API)	200	200
Starch (disintegrant)	50	50
Na alginate (retardant)	-	235.6
Bentonite (binder)	236.5	0.105
Mg stearate (glidant)	1.3	1.3
Talc (lubricant)	12	12

Characterizations of carbo tablets

The tablet was examined for a number of parameters using classical, pharmaceutical and instrumental characterization.

Pharmaceutical characterization

Bulk and tap densities: A quantity of 2 g from each of the powdered samples was placed in a 10 mL cylinder and the volume, Vb, occupied by each of the samples without tapping was noted. After 10 taps on the table, the occupied volume Vt was read. The bulk and tap densities was calculated.

Granule friability: The friability of the granules was examined using a friability tester (model 903, China). After the granules with a size of more than 14 mesh (1 g) is rotated at 25 rpm for 5 min, and the amount of the granules maintaining a size of more than 14 mesh was

measured. The weight loss (%) of the granules from the initial amount is calculated as friability [6, 12].

Tablet strength: The side of the cylindrical tablet was sandwiched softly between the ‰ at platens of a massanto hardness tester, Uk. Then, the stress was gradually increased, and the hardness (F, kg) was measured. Tensile strength (St, kg/cm^2) was calculated using the Equation 1.

$$St = \frac{2F}{pxDxT} \quad (1)$$

Where D and T are the diameter (cm) and thickness (cm) of the tablet, respectively [6, 12].

Disintegration time of tablets: As the medium was blackened by the tablet disintegration, the disintegration time was determined by the normal disintegration apparatus. A Model ZT disintegration tester was used, a basket with a mesh size of 1.5 mm in the disintegration apparatus is moved up and down with a distance of 5.5 cm at 30 strokes per min at 37 °C, when the bottom of the basket moved up to the surface of the test medium, which enabled me to observe the status of the tablet on the basket. The time taken for the tablet to completely disappear from the basket is measured as a disintegration time. Water was used as a test medium [12].

Instrumental characterization

Differential scanning calorimetric (DSC) studies

DSC studies for the commercial carbo tablet and the prepared tablet was analyzed to evaluate the polymorphic changes in the drug as well as its interaction with the excipients. Samples of pure drug and powdered tablets were weighed directly in pierced aluminum pans and scanned from 25 °C to 190 °C at a heating rate of 10 °C/min under the static nitrogen gas at a pressure of 20N on aluminum 40 micro liter/mL and flow rate of 50 mL/min flow rate. Mettler Toledo STAR software was utilized to collect and analyze the data [14, 15].

Scanning electron microscopy (SEM) analysis

SEM was used to study the morphology of the synthesized carbo tablet. This was carried out using the FEI ESEM (S-3400N) coupled with EDX-SEM analysis [2, 15] .

Fourier transform infrared spectroscopy (FTIR)

MC powder, carbo tablets, CCT, and the spent carbo tablet mixture each individually analyzed. The samples were mixed with potassium bromide in approximately 1:100 ratios and formed into a pressed disc. The resulting disc was placed in a vacuum to expel air trapped between particles [14, 15].

Adsorption experiments

Batch adsorption and kinetics experiments

The adsorption of acetaminophen was characterized at 37 °C as follows: Carbon tablet and emzor were added to the simulated gastric fluid solution in the ratio as stated in the batch adsorption preparation, and stirred at 90 rpm using a magnetic stirrer for 5 min and at varying interval of time for kinetics studies, and examined by Uv-vis spectrophotometer to determine the concentration of free acetaminophen. Procedures for the effects of parametric factors were carefully followed [2, 3].

Batch adsorption studies

Acetaminophen adsorption can be calculated at equilibrium as shown in Equation

$$Qe = \frac{(Co-Ce)}{m}V \quad (2)$$

where Qe is the amount of acetaminophen adsorbed (adsorption capacity) per gram of the adsorbent at equilibrium (mg/g or ppm); Initial *(Co)* and final equilibrium (*Ce*) concentration of acetaminophen in solution in mg/L; V (L), volume of solution and the amount of adsorbent in grams [2, 16]. Removal (adsorption) efficiency of the carbo tablet samples were calculated from the Equation 3 [16].

$$\% RE = (\frac{Co-Ce}{Co})X\ 100 \quad (3)$$

Results and discussion

Physical inspections of formulated carbo tablets

The pictorial representation of (a) Formulated Carbo Tablet (FCT), (b) Formulate carbo tablet with Alginate (FCT-Alg), (c) Commercial carbo tablet pack, (CCT pack), (d) Commercial carbo tablet (CCT coated), (e) FCT and (f) CCT (uncoated) is given in Plate 1. The shape, size and diameter of the tablet were adequate considering the nature of the excipients used. The striking difference between the derived and commercial CT is the technology involved in polishing the drug surface.

(a) (b)

Plate1. (a) Formulated (FCT) and (b) Commercial (CCT) carbo tablets.

Physicochemical parameters of carbo tablet

Results of the physicochemical characterization of FCT, formulated by wet granulation method based on USP 30 Pharmacopeia were reported as mean value and presented in Table 2. The size, hardness, and disintegration characteristics of the tablets are shown in Table 2. These values were considered adequate for strength and disintegration [6]. The size, thickness and diameter of the tablet is due to the compressibility nature of the bulking agents when subjected to high.

The encapsulation efficiency of the tablet was 90.58% which shows the quality and compatibility of the binder, bentonite as the bulking agents in compliance with Ilomuanya *et al*. [2].The tablet failed friability test but pass the disintegration test because of the release retardants. The disintegration time was prolonged in FCT-Alg. because the additive is a release retardant, Na alginate. At a shorter time, API was release from the drug, but at more water uptake, matrix were formed, Na alginate in these scenario acts as thickener, gelatin or as chelators therefore suitable for control of overdose and intoxication by reducing re-absorption of toxic substance into the body as evident in the literature [17]. The 500 mg drug was formulated to test the adsorption profile of FCT-Alg., which at the preliminary stage, was said to remain in the system for a longer time, during which, any adsorbed molecule (toxins, heavy metals, and poisons) should have been eliminate before reabsorption back into the body [17]. According to Sougata and Subrata [18], Na alginate forms insitu hydrogels (with water) under physiological conditions (such as temperature and pH). In 1966, the national Institute of Health published findings that Sodium alginate in specified doses was capable

of reducing absorption of some toxins when in these sense it is used as a chelator [17].

Table 2. Mean Values of Characterized FCT Formulated by Wet Granulation Based on US Pharmacopeia.

s/no	Parameter	Unit	Value
1	Repose angle	Degrees	30.00
2	Bulk density	g/cm^3	1.02
3	Tapped density	g/cm^3	1.30
4	Encapsulation efficiency	%	90.58
5	Thickness	cm	0.30
6	Diameter	cm	1.2

Pharmaceutical characterization of carbo tablets

Pharmaceutical characterization of the formulated carbo tablet, based on USP Pharmacopeia is given in Table 3.

Table 3. Mean Pharmaceutical parameters of FCT and CCT Based on US Pharmacopeia.

S/No	Tablet Parameter	Unit	Mean values		
			FC(Alg)	(FCT)	CCT
1	Tablet Strength	KJ	5.65	6.61	7.45
2	Crushing Strength	KJ	4.8	6.72	7.10
3	Friability	%	7.00	3.10	2.20
4	Disintegration time	Min	90	3.40	3.10
5	Drug category	-	SDT	FDT	FDT

FDT- Fast disintegration tablet, SDT- slow disintegration tablet. FCT-formulated carbo tablet, CCT-commercial carbo tablet, FCT-Alg – Formulated carbo tablet with Na alginate.

FTIR characterization of carbo tablet

The active sites (functional group) of the adsorbent (carbo tablets) were investigated using the FT-IR spectrometer (Agilent technologies, model 4000-650). The results are presented in Figure 3 for the formulated and spent carbo tablets. Table 4 shows the interpreted comparative FT-IR spectral characteristic of carbo tablet. Peak distortion from 3876.4 cm^{-1} of FCT to 3321 cm^{-1} of spent CT indicates surface interaction between the adsorbent and the adsorbate. Comparing FCT with FCT –Alg, it can be noticed in Table 4 that, FCT showed hydroxyl group, at 2083.6, OH stretching of COO-, stretching of C-O at 1103.3 while FCT-Alg has an important amine peak at 3876.4 and a C=O of amide peak at 643.8, bending of (C-H) group at 730.6-752.9, stretching of (O-H) group at 2877.5, and stretching vibration of (C=C) at1584.1. Spent CT has almost the same spectral identification with FCT-Alg with vibrations of (C-H) stretch at 1435, N-H bending vibration at 1505.8 and broad (OH) band at 3652.8 of alkyl chains and CHO. Comparing FCT with CCT, it is noticeable that CCT has an important vibration at (=C-H stretch) 995.2 of alkene group and a =C-H at 2650.6 courtesy of the alkyl group. The different level of vibrations and the uniformity of FCT and CCT

are indicative of high degree of hydrogen bonding.

Several characteristic vibration bands can be noticed in Figure 3. Sample (a) showed hydroxyl group, carbonyl, bending of (C-O) group, stretching of (N-O) group, and stretching vibration of C=C with almost the same spectral identification of asymmetrical and symmetrical vibrations of (C-H) and broad (OH) band indicated high degree of hydrogen bonding [19].

Table 4 presents less vibration modes due to the excipient compatibility and less interference of excipients with the API. Adsorption may also have been influenced by the functional groups associated with the surface of the carbo tablet. Excipient interactions with the functional group on the surface of the CT leads to variation in values and this accounts principally for the lower values obtained from FCT-Alg, as this was formulated with the most excipient %w/w concentration. This associated interaction lends credence to the reduced acetaminophen adsorption density observed in the SEM, Plate 2(a). Excipients utilized in the formulation of the activated charcoal tablets act as deterrents to acetaminophen adsorption as they may contribute either acidic or basic functional groups to the surface of the activated charcoal leading to an interaction between the adsorbent and adsorbate functional groups thus making the micro and macro pore surfaces unavailable for adsorption [2].

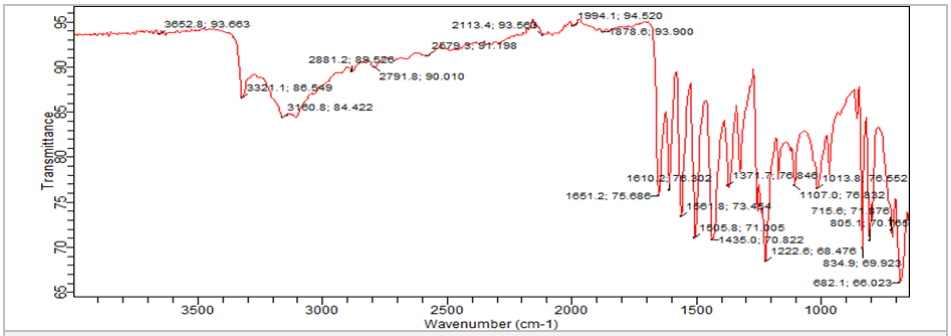


Figure 3. FTIR spectrum spent carbo tablet.

Table 4. FTIR Spectral Interpretation of Commercial and Formulated Carbo Tablets.

Group Freq. (cm^{-1})	Functional group	Observed Frequencies (cm^{-1})				Assignment
		FCT-Alg	FCT	CCT	Spent	
1000-690	Alkane, alkenes	730.6, 752.9	690.9	995.2	715	C-H, =C-H bend
1240-1050	Amine	-	1103.3	-	1107, 1222.6	C-O stretch, sec. amine
1450-1250	Alkanes, ethers	1349.3, 1412,7	-	-	1435,	C-H stretch, C-O stretch; CH_3 symmetric deformation; N-O
1640-1550	Amine, alkyne, alkene, aromatic	15841.1	-	-	1505.8, 1610.2	N-H bend; C≡C stretch; C=C stretch
2050-1650	Aromatic,	1643.8, 1990.4	1599.0	1994.1	1651.2, 1994.1	N=N=N, Anti-symmetric stretch; C≡C
2450-2250	Amine, alcohols	2325.9, 2467.5	-	-	-	N-H , O-H

3000-2500	phenols	2877.5	2918.5	2650.6	2579.3, 2881.2	O-H broad; O-H stretch; -NH stretch; ≡CH-H stretch
3800-3000	Amine, alcohols	3876.4	-	-	3321.1, 3652.8	O-H broad; O-H stretch; -NH stretch; ≡CH-H stretch

Differential scanning calorimetric (DSC) characterization

The heat flow pattern and sorbent compatibility were investigated using DSC analysis. Metler Toledo star software was used to collect and analyze the data. Figures 4a and b demonstrates the heat flow pattern for the FCT and CCT. Results are indication of good heat transfer, which may be attributed to the porous nature of the carbon tablet synthesized. The Dsc results (Figure 4a) revealed that the formulated carbo tablet is 99.35 ± 0.207% . Compatibility study shows early peak at 158.62 °C as against the 161.66 °C expected for melting during endothermic heat transfer of carbon.

Figure 4b is the DSC Thermogram for CCT. its purity value is 100.00 ± 53.296 % with early onset peak at 75 °C as against the 114.76 °C required for endothermic heat transfer of carbon. The results were found to be similar to the research carried out by Wyasu *et al*. [20]. The heat transfer pattern and heat flow through the activated carbons tablet were studied. Heat transfer measured for FCT was generally high due to low porosity, small surface area and discontinuity of the carbon structural framework. The Na alginate formulations interferes with porosity as evident in the SEM image. Contrary to this observation is the result of CCT due to high porosity, large surface area and continuity of the carbon structural lattice.

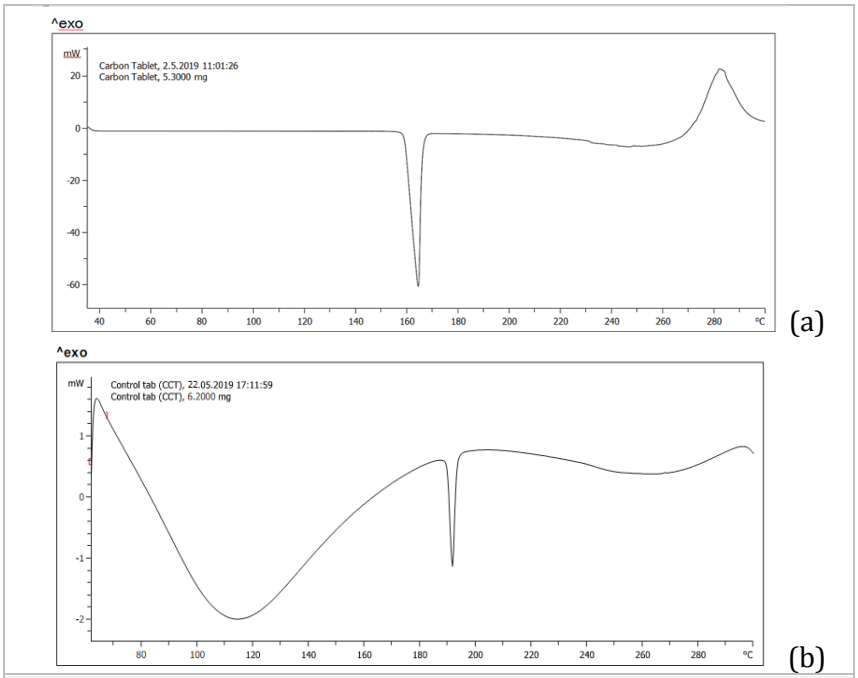
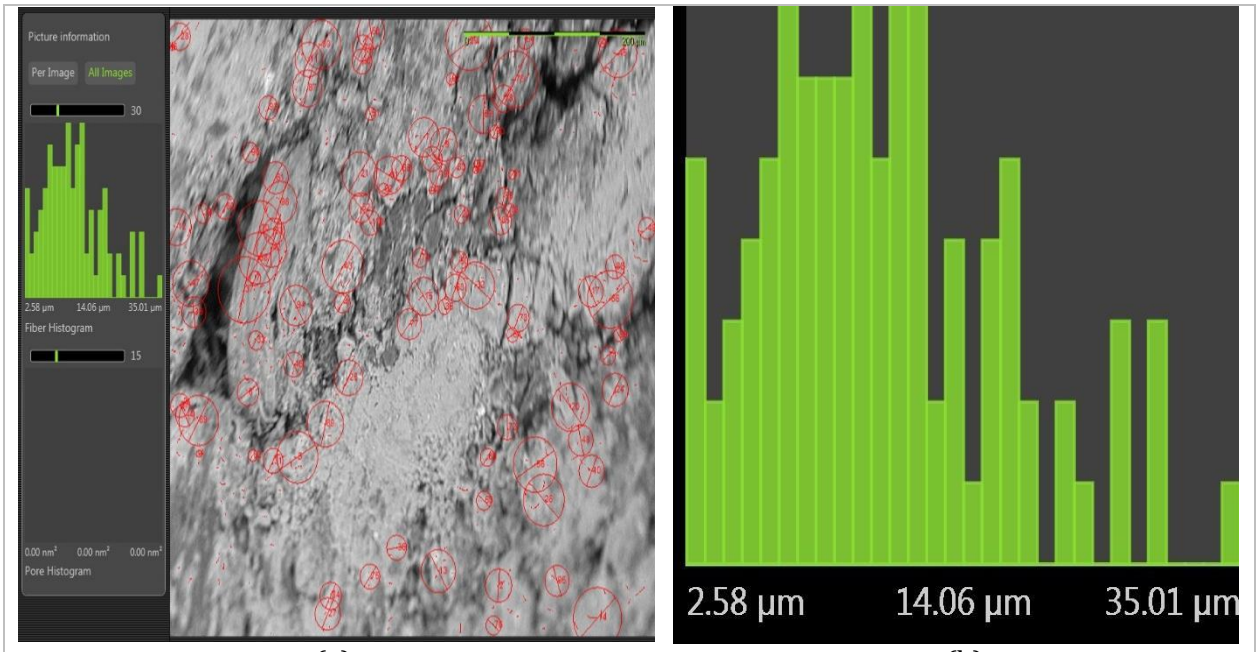


Figure 4. DSC Thermogram of (a) FCT and (b) CCT.

SEM characterizations of the derived carbo tablet

The surface morphology of the formulated carbo tablets was studied using scanning electron microscope. Plate 2 shows the SEM images for the (a) FCT and (b) FCT-adsorbed excipient. The obtained results clarified that the formulated carbo tablet has pores spaces and have been mostly occupied by Na alginate. This character conjugated with size and shape irregularities was clearly seen with the spent carbo tablet. SEM images revealed that, the adsorption did not take place on the surface of the activated charcoal tablet as the adsorption sites were unavailable for acetaminophen adsorption Plate 2a, microscopic studies revealed that adsorption of acetaminophen occurred on the microporous pores of the tablet, with increased adsorption densities seen, this is in consonance with Ilomuanya *et al*. [2]. It was found that, the presence of excipients in the tablet formulation greatly hampered adsorption onto available sites (Plate 2a), surface coverage was minimal, the tablet formulation showed more acetaminophen adsorption. The SEM fibermetric image (Figure 2b) of the FCT depicted that the particles are aggregates, with irregular crystalline structure within the < 50 µm range. Physical adsorption of the minute particles with lumped edges was found on huge background.



(a) (b)

Plate 2. SEM (a) Fibermetric Image of FCT-Adsorbed excipient and (b) Fiber Histogram of FCT Showing Average Particle Sizes.

EDX SEM characterizations of the formulated carbo tablet

The chemical composition of the formulated carbo tablet was detected using the EDS/SEM analysis. Figure 5 and Table 5 present the qualitative and quantitative results, respectively. EDAX results provided additional understanding of the surface material. EDX analysis was used to acquire the elemental composition of a sample and allows for a more

quantitative result than that provided by only SEM analysis. Combination of SEM and EDX analysis offered chemical composition and elemental investigation, providing a comprehensive metallurgical evaluation. The chemical compositions are given in Table 5. As seen from the peak, Ca, Si, K, Fe, Ti, and Al were on a high concentration. The position or distribution of each element depends on the active or binding sites occupied. Other elements are P, S, Zn and Mg. Primary elemental composition material is O, and H disabled because the Na alginate structure is closed-packed sheets of O atoms with H in interstices spaces.

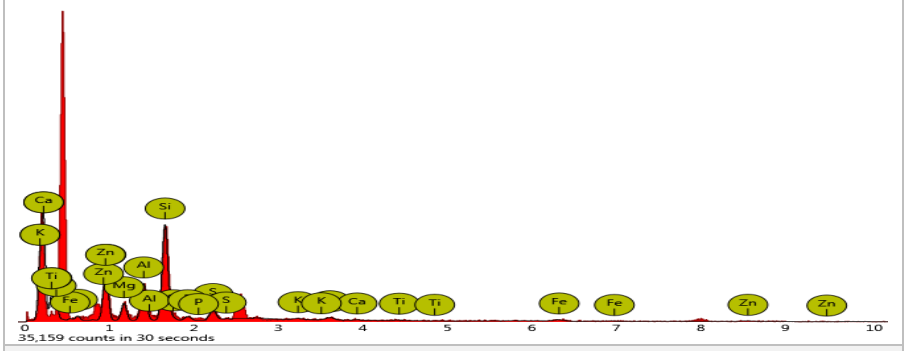


Figure 5. EDS spectrum of FCT.

Table 5. Elemental Composition of FCT from the EDX-SEM.

Atomic Number	Element Name	Atomic percentage (At.%)	Weight percentage (Wt.%)
14	Silicon	41.36	41.01
11	Sodium	21.50	17.45
13	Aluminium	15.62	14.88
12	Magnesium	7.72	6.63
16	Sulfur	5.14	5.82
26	Iron	2.24	4.42
30	Zinc	1.50	3.46
15	Phosphorus	2.37	2.59
20	Calcium	1.43	2.02
22	Titanium	0.55	0.94
19	Potassium	0.57	0.79

UV visible quantification and batch adsorption study.

UV Visible characterization of the formulated carbo tablet, FCT, formulated carbo tablet with Na alginate, FCT-Alg and commercial carbo tablet CCT were simulated in the gastric fluid. Figure 6 reveals the charts for the effect of some parametric factors (carbo tablet dosages, PCM dosages, contact time, and pH) on adsorption of acetaminophen in SGF. The profile of the adsorption of acetaminophen by the carbo tablet was examined using a magnetic stirrer at 90 rpm and 37 °C and UV-vis spectroscopy. Under this condition, the tablet could move sufficiently in the medium without spattering out of the medium. The adsorption profile was obtained with a ratio of acetaminophen to medicinal carbon tablet of

0.1: 0.1- 0.5 (w/w) in SGF, at pH 1.2 and pH 6.8 in water. The adsorption occurred rapidly, and was almost completed within 5 mins. The extent of adsorption hardly differed among the solvents. The difference in adsorption could not be explained by simple factors such as solvent pH. In addition, the extent of adsorption at equilibrium was investigated by changing the concentration of acetaminophen added. The extent of adsorption reached a plateau when the concentration of acetaminophen added was raised. It is possible that additives such as Na alginate affect the adsorption potential of medicinal carbon tablet as described by Nakamura *et al*. [21].

Effect of initial concentration

The RE (%) of CT in the sample is influenced by the initial concentration of adsorbate. The highest percentage removal by FCT was 99.17% in SGF and 81.57% with water. Thus, at higher initial concentration, the percentage removal decreases. This could be linked to competition for attachment sites [3, 19].

Effect of carbo tablet dosages: It can be noticed that, the adsorption capacity enhanced as the dose of carbo tablet was increased. However, this trend was not observed in the samples where tablet was formulated with sodium alginate (FCT-Alg.), as the retardants occupies the space that could have been active sites for adsorption, as evident on SEM micrograph (Plate 2) [2]. Although the alginate has adsorptive characteristics by itself [22], it is not comparable to that of the activated carbon. When the amount of dose is increased, the surface area exposed to the adsorbate is increased. There are vacancies, where the adsorbate is in direct contact with the binder instead of the more adsorptive carbo tablet. It was observed that increasing the dosage of carbo tablet enhanced the adsorption capacity and removal efficiency; however, opposite direction was observed for the carbo tablet formulated with Na alginate. This is due to the chaleting properties of the alginate as it form gel at the presence of water that reduced the number of adsorption sites [22]. By increasing the dosage from 0.1g to 0.6 g for FCT, the removal efficiency improved from 90.82% to 92.8%, CCT increased from 89.17% to 96.46%, while the FCT-Alg decreased from 99.17% to 63.18%. The decrease in the percentage removal for FCT-Alg may be due to the unavailability and insufficient active site for adsorption of acetaminophen [17, 19].

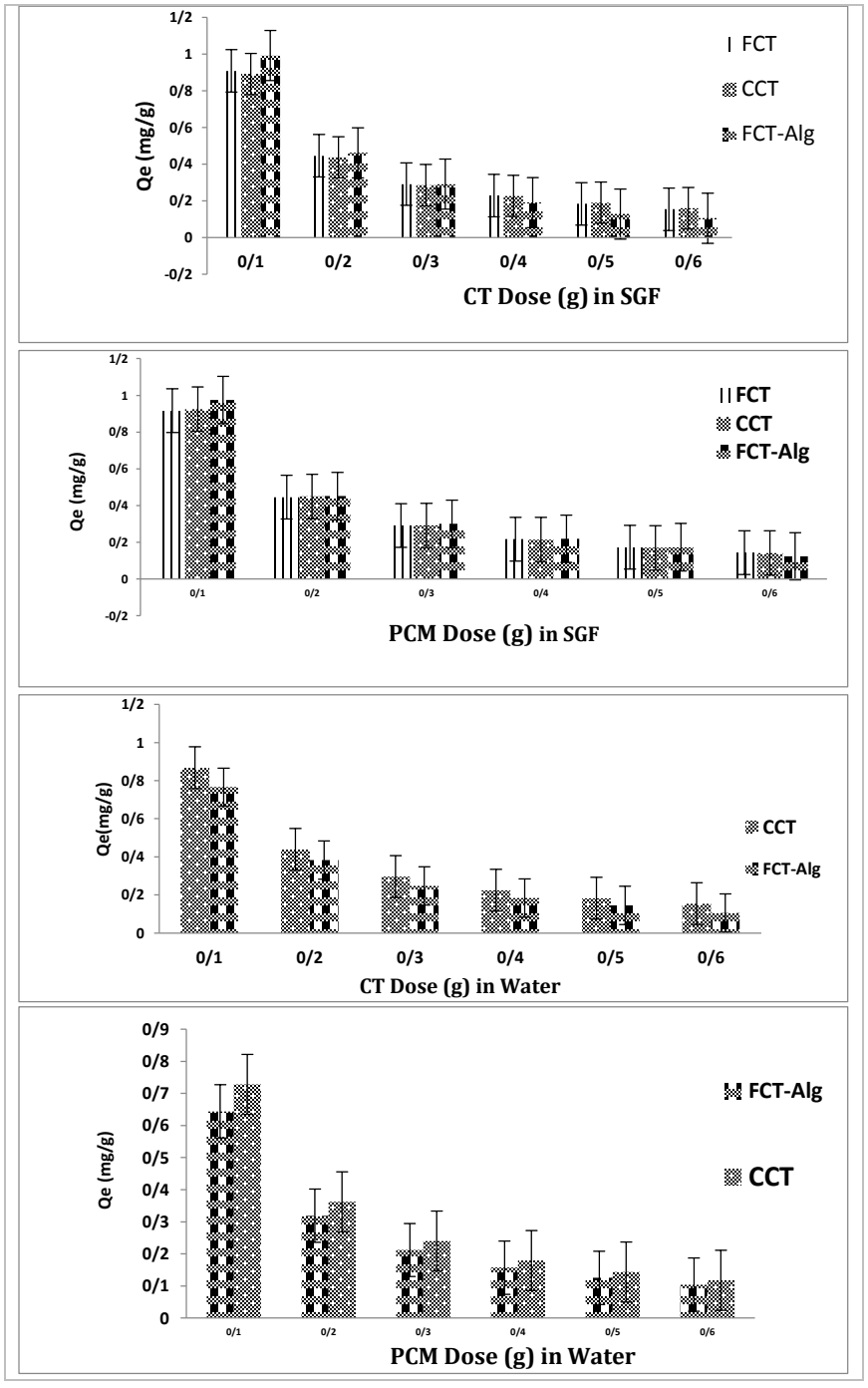
Effect of PCM dosages

When the amount of dose of PCM was increased at fixed FCT and CCT with time (Figure 6), the surface area (exposed to the adsorbate) was reduced. PCM occupies the space that could have been active sites for the adsorption. It reached a plateau and started decreasing due to the effect of the alginate and high dose of the PCM. It was also observed that, increasing the dose of the PCM resulted in having less active site for the adsorption by carbo tablets.

Effect of contact time

Adsorption decreased with increasing the contact time. When the contact time was increased from 3 min to 18 min, the removal efficiency reduced from 91.67% to 65.68% for FCT, and 95.44% to 66.58% for the CCT. These results were in agreement with the other reports [17, 21]. Adsorption was seen faster at shorter time for all samples, this may be due to the possibility of desorption setting in at longer time, molecules also clump together, forming matrix especially for the FCT-Alg formulations, which closes or block adsorption sites of the activated carbon tablets, the presence of some excipients especially bentonite and alginate can

also reduce adsorption at longer time in accordance with the report of Ilomuanya *et al*. [2]



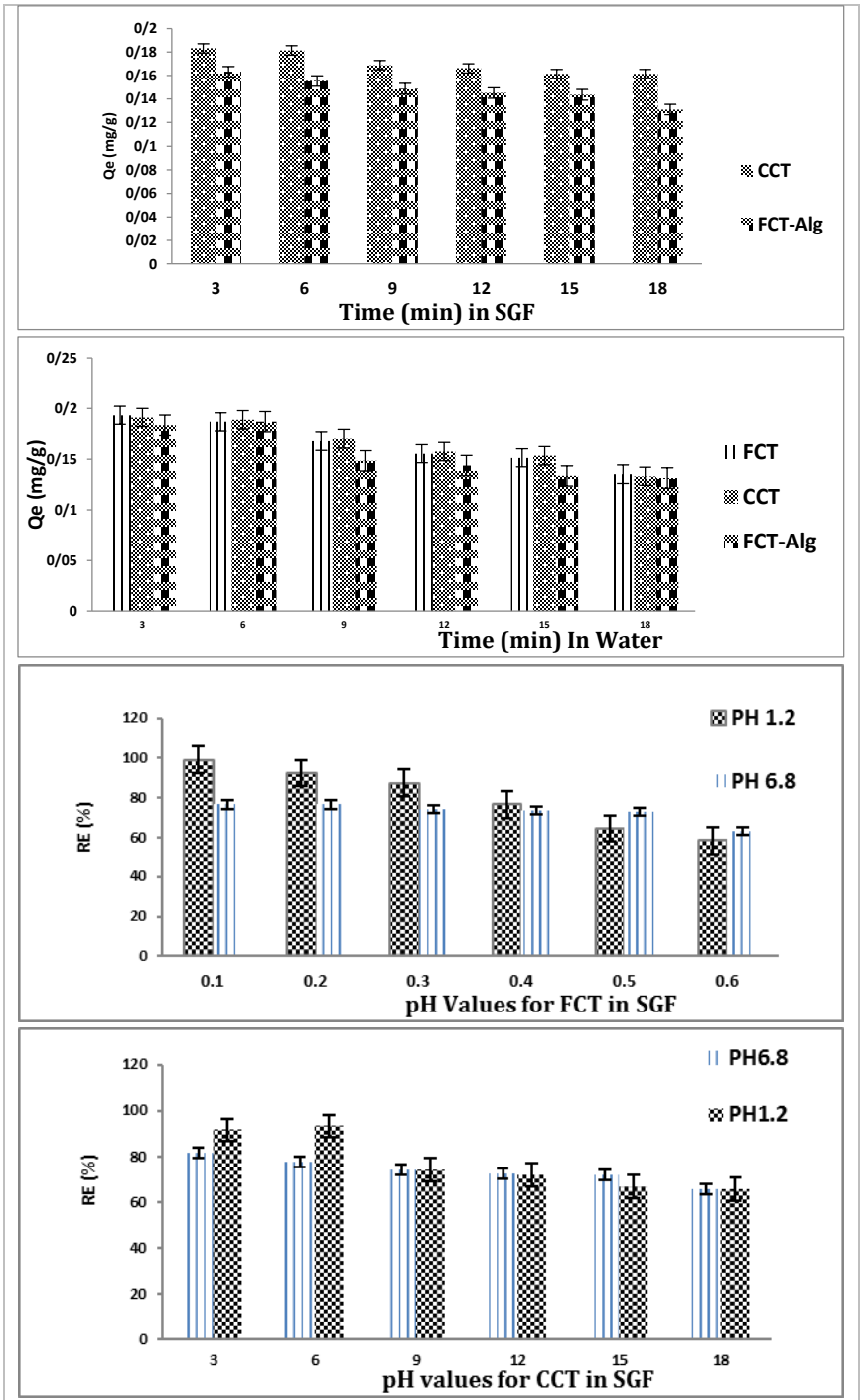


Figure 6. Effect of Parametric factors on the adsorption of acetaminophen in SGF and in water.

Effect of pH

pH of the adsorbate/adsorbent solution has been identified as the most important parameter governing adsorption by different adsorbents. This is partly due to the fact that the solution pH influences the chemical speciation of ions. The effect of pH on adsorption of

acetaminophen onto formulated carbo tablet is demonstrated in Figure 6-d. At low pH, the adsorption capacity was low due to the increase in positive charge density (protons) on the surface site, resulting in electrostatic repulsion with positive charges active site on the surface. Electrostatic repulsion educed with increasing the pH because of the reduction of positive charge density on the edges, which resulted in an increase in adsorption on the surface of the material. In an alkaline medium, the surface becomes negatively charged [19]. The removal efficiency of carbo tablet in SGF (pH 1.2) reduces from 99.17% to 76.58%. In water (pH 6.8), %RE reduces from 96.46% to 92.46% for CCT. At pH 1.2 for SGF, the amount of acetaminophen adsorbed per gram of adsorbent, (FCT-Alg., FCT, CCT) at equilibrium (mg/g) is higher, compared to adsorption at pH 6.8 in water. This shows that pH 1.2, which is the pH of the gastric compartment, is where adsorption takes place at optimum temperature, this agreeing with other takes [2, 6].

Comparative study

Table 6 depicts the results for the statistical test of significance, carried out using one factor ANOVA to compare the adsorption efficiency of the adsorbents.

Table 6. Comparing the level of significance between FCT, FCT-Alg and CCT for Acetaminophen uptake at 95% Confidence Interval.

Carbo tablet	Parametric Factors	P-Value	Test of Significant (based on %RE)
FCT	Concentration	0.788685	Not Significant
	Time	0.001674	Significant
	pH	$1.92x10^{-05}$	Significant
	Dosage	0.931478	Not Significant
CCT	Concentration	0.588683	Not Significant
	Time	0.003663	Significant
	pH	0.003663	Significant
	Dosage	0.931478	Not Significant
FCT-Al	Concentration	0.886856	Not Significant
	Time	0.003663	Significant
	pH	$1.92x10^{-05}$	Significant
	Dosage	0.134872	Not Significant

Table 6 shows the level of significance ($p<0.05$) between FCT, FCT-Alg and CCT for different parametric factors at 95% confidence intervals. The results revealed that, the p-Value for the acetaminophen adsorption was not significant for the effects of concentration and dosage. An exception to this is pH and time, whose values were greater than 0.05, depicting significance for effect of pH and time on the sorption by CT when compared to sorption by CCT. In essence, factors such as time and pH had significant effect on adsorption as evident from disintegration time and strength of tablet.

Conclusion

In this research study, carbo tablets were produced as compact dosage form by the wet granule compression method. The tensile strength and disintegration time were found to be acceptable. The adsorption potential of the tablets was lower to some extent when the formulation was incorporated with sodium alginate. The DSC analysis provided us useful

information about the heat energy transfer through the carbo tablet produced. The derived carbo tablets acted as a high performance adsorbent for the detoxification of acetaminophen (paracetamol) overdose in both simulated gastric juice and water media, with over 90% detoxification efficiency.

Conflict of interest

We have no conflicts of interest to disclose.

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