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Synthesis, Size Characterization and Catalytic Application Studies on the Biostabilised CuO Nanocubes for the Oxidation of Drugs with pH and Mass Effects

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Abstract- Drug polluted waters are treated by various methods. Among the chemical methods the advanced **oxidation** process is adopted in this work using copper oxide nanocubes stabilized with green polymers namely chitosan and starch. Copper oxide nanocubes (CuOnc) are characterized using FTIR, FESEM and HRTEM. The edge side length of nanocubes of starch and chitosan stabilized CuO are found to be 10 ± 1nm, 8 ± 1 nm respectively. H_2O_2 is used as the oxidant. Time dependant UV spectra for the oxidation of the three drugs namely gentamicin (GE), furosemide (FU) and deriphyllin (DH) are studied under the pseudo first order conditions, using the Cuonc as the catalyst. Based on the absorbance versus time plots, the kinetic plots for the rate coefficient determination are made. The optimum pH values for the maximum rate coefficient values for the three drugs are found to lie within the range of pKa values. The catalyst mass effect was studied and 1mg of CuOnc has been found to be effective. The trend observed in the rate coefficient values for the oxidative degradation for the three drugs is GE>FU>DH and chitosan stabilized CuOnc is found to catalyse better than the starch stabilized ones for the oxidative degradation of the drugs.

Index Terms- advanced oxidation process, biostabilisers, CuOnc, kinetics, mass effects, pH

I. INTRODUCTION

Metal oxide nanoparticles of transition metals possess unique and enhanced properties, which include optical, magnetic, semiconducting, catalytic [1], etc., due to enormous increase in surface area to volume ratio values compared to the bulk materials. The preparations [2], size [3] and shape [4-9] controls and characterization of metal oxide nanoparticles, possess considerable practical importance in the potential science of catalysis [10]. Biostabilisers when used in the metal oxide nanoparticles synthetic method, a greener and cost effective catalysis can be invoked. Copper oxide being one of the cheapest and abundant transition metal oxides available, the nanoparticles of CuO stabilized with biopolymers certainly can bring about green catalysis of oxidation of organics. Potential therapeutic drugs which are organic substrates, though find medicinal applications, there is an inevitable enviroaquatic pollution caused due to the chronic and high dose discharges from hospitals, pharmaceuticals etc. Drug polluted waters tat pose threat to aquatic life system [11-13], sometimes leak its way into the public water distributing system. Therefore it is essential to treat water polluted with drugs, suing advanced oxidation processes (AOP) that employ biostabilised metal oxide nanoparticles as the oxidation catalysts. This effect may ensure an efficient, quick and higher turnover method.

In the present work, CuO nanocubes are synthesized by coprecipitation method, using chitosan and starch as the biostabilisers [14, 15]. Chitosan with 90% deacetylation having medium molecular weight sample was used. Size and shape characterization of nanoparticles are investigated using FTIR, PXRD, FESEM and HRTEM. Incidenttally, nanocubes of CuO are detected in both the stabiliser system and 10 ± 1nm, 8 ± 1 edge lengths of nanocubes are obtained from starch and chitosan biopolymers respectively. In recent years, drugs such as furosemide (FU), $C_{12}H_{11}Cl\ N_2O_5S$: 5-Amino sulphonyl-4-chloro-2-furanyl methyl acid ; gentamicin (GE), $C_{21}H_{43}N_5O_7$: (3R,4R,5R)-2-([1S,2S,3R,4S,6R)-4,6-diamino-3(2R,3R,6S)-3 amino-6-[(1R)-1-(methyl amino)ethyl]oxan-2-yl]oxy]-2-hydroxy cyclo hexyl]oxy)-5-methyl-4-(methyl amino)oxane-3,5 diol; and deriphyllin (DH), $C_{11}H_{19}N_5O_4$: 1,3dimethyl-7H-purine-2,6-dione;2-(2-hydroxy ethyl amino)ethanol, are used widely for the treatment of edematous states [16-18], serious suppurative antiseptic process[19,20] and bronchi dialysis [21,22] respectively, which exist commonly, world wide . Therefore such drugs are used profusely and hence, detected in alarming levels in the environmental aquatic effluents. In this work, we report an investigation on the utilization of CuO nanocubes synthesized with biostabilisers, as green catalysts for the oxidative degradations of the drugs FU, GE and DH in aqueous medium. In Figure 1, the molecular structures of the drugs are given. Hydrogen peroxide has been used as the oxidising agent. In the absence of the catalyst, the oxidation of the drugs proceeded for more than 48 hours in presence of H_2O_2. Therefore, incorporation of CuO nanocubes was adopted and an effective oxidative degradation of the drugs was found to be complete within one hour time of reaction. Adopting the time dependant UV spectra, the rate coefficients of the oxidative process of the drugs are determined. From the absorbance variation with time data kinetic plots are made under pseudo first order conditions. CuO nanocubes with chitosan as the stabilizer produced higher rate coefficient values than the starch stabilized ones. The optimization of the reaction

conditions are found out from the effects of medium pH and catalyst mass (feed) on the rate coefficient values. The salient features of the results are discussed.

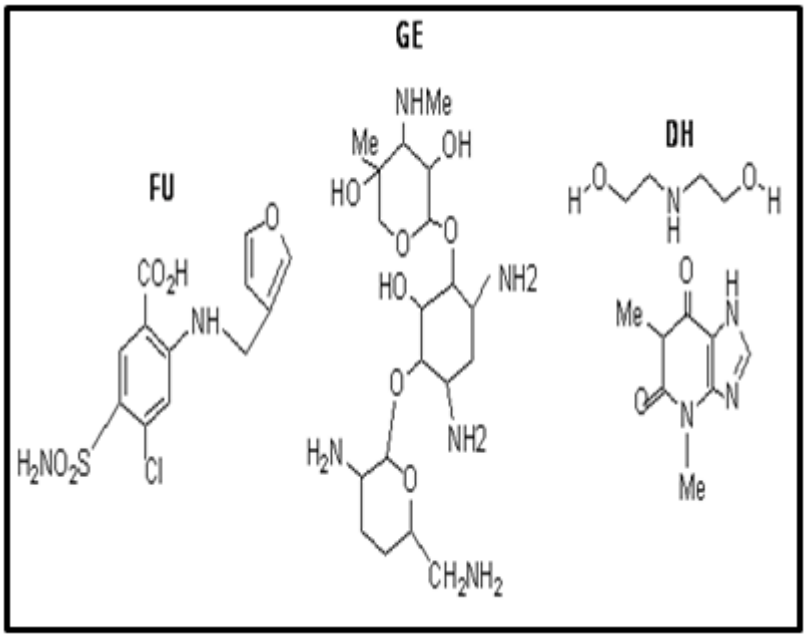

Figure1: Molecular structures of the drugs FU: Furosemide, GE: Gentamicin and DH: Deriphyllin

II. MATERIALS AND METHODS

1) Materials

Deriphyllin, furosemide and gentamicin were purchased from Cadia health care, Abbot health care, Aventis pharmacy, India. Sodium hydroxide and copper nitrate were purchased from S.D Fine Chemicals Ltd., India with 99.9% purity. Triple distilled water was used in all solution preparations. Starch, chitosan with 90%deacetylation and hydrogen peroxide (30% w/w) were analar grade and purchased from Loba Chemie Ltd., India.

2) Preparation of CuO nanocubes

Into a three necked 100ml capacity round bottom flask, 10ml of 1mM copper nitrate solution was added through one neck and into the other 5ml of 1.5% by weight aqueous solution of chitosan was added and freshly prepared 0.02M sodium hydroxide was added drop wise until the color of the solution changes from yellow to brick red and then to black with continuous stirring and then kept in microwave oven for 8min (10% power) [2]. Then the black powder CuO so formed was washed with water, filtered and dried. Mechanism for the formation of CuO nanocubes may be follows [3]

$$Cu^{2+} \xrightarrow{2OH^-} Cu(OH)_2 \xrightarrow{2OH^-} \left[Cu(OH)_4^{2-}\right] \overset{\text{chitosan/starch}}{\rightleftharpoons} CuO(\text{nanoparticles}) + 2OH^- + H_2O$$

3) Size Characterization of CuO

FTIR spectra are recorded in Ker pellets for the pure capping agents, chitosan, starch and chitosan-CuOnc and starch- CuOnc at 25^0C using Bruker Tensor 27 instrument. FESEM photograph of the chitosan and starch stabilized CuOnc are measured using Hitachi SU6600 instrument. The HRTEM photograph was taken on a PHILIPS CM20 model instrument operated in the accelerating voltage of 120 KV using a Formvar coated copper grid.

4) Reaction catalysis

Into a double walled 50ml capacity, magnetic stirrer attached reaction vessel,1mg of freshly prepared CuOnc and 10ml of the 1mM drug solution at pH=7.0 (maintained by addition of buffer tablets) was mixed and into the other neck 0.5ml of 0.01M H_2O_2 was added drop wise with the contents being stirred continuously. The inception of the reaction was considered from the time of addition of H_2O_2. Additions were completed within 30 sec and small aliquots of the sample are drawn out at regular intervals of time (5min)

and subjected to UV spectra scan. The completion of the reaction was noted with the gradual decrease in the absorbance falling to the base line. For the pH effect studies the drug and H_2O_2 solutions are prepared in various pH solution maintained with buffer tablets. The catalyst mass effect was studied by repeating the above procedure with different catalyst feeds

III. Results and Discussion

A. FTIR characterisation

In the Figure 2 FTIR, spectra of pure chitosan, chitosan-CuOnc, starch and starch-CuOnc are given. Although the possibility of overlapping peaks between N-H and the O-H stretching in the region 3000,3500cm^{-1} occurs in pure chitosan spectrum , inFigure 2a the IR spectra of chitosan-CuOnc a significant decrease in the transmittance in the region, indicates that, the N-H vibrations of chitosan are affected by the binding of copper. Also, shifting of the N-H bending vibration band at 1578 cm^{-1} to 1582cm^{-1} accompanied by diminishing of intensity ascertains the interaction between chitosan and CuOnc. IR band s at 585 cm^{-1}, 535 cm^{-1}, 480 cm^{-1} can be attributed to the Cu-O stretching vibration of the monoclinic phase of CuO [5]. There is no peak at 615 cm^{-1} confirming the absence of Cu2O and indicating the formation of CuO. In Figure 2c the two peaks at 1650 cm^{-1}and 1160 cm^{-1} are caused by the O-H bending and C-O stretching. The peaks in the range 1460 cm-1 are attributed to the C-H bending vibration of the HC-CH- links of pure starch molecules. Figure 2d depicts the IR spectra of starch-CuO. The absorption peaks at 1160 cm^{-1} and 1650cm-^{1} been shifted and peaks at 590 cm^{-1}, 537 cm^{-1}, 477 cm^{-1} are the characteristics of Cu-O bond formation .

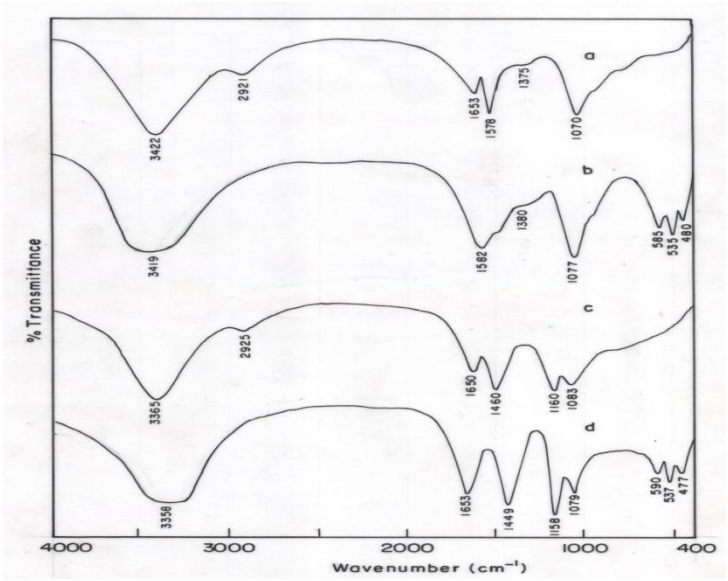

Figure 2: FTIR of (a) chitosan, (b) chitosan-CuOnc (c) starch (d) starch-CuOnc and at 25^{o} C

B. FESEM and HRTEM studies

In Figure 3 FESEM of chitosan-CuOnc and starch-CuOnc are shown the nanoparticles are found to be cubical and nearly monodisperse. In Figure 4 the HRTEM photographs of chitosan-CuOnc and starch-CuOnc are given and the mean particle size was found to be 8±1nm, 10±1 nm respectively.

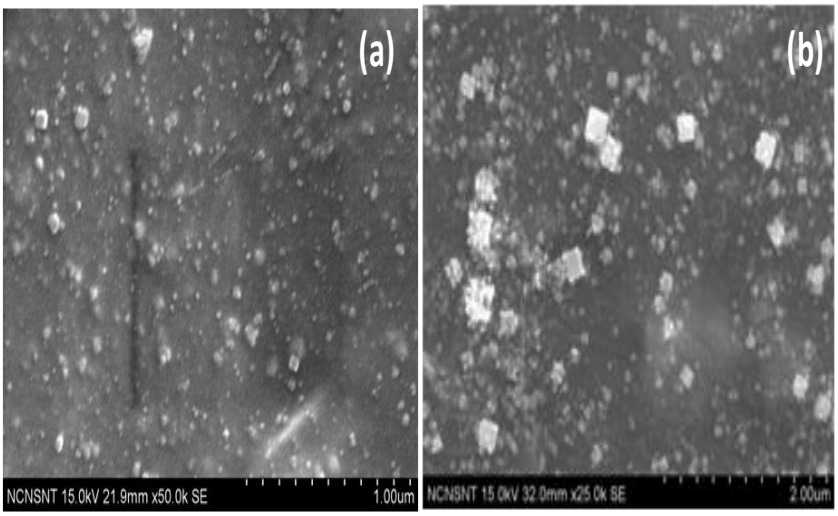

Figure3: FESEM of (a) chitosan-CuOnc and (b) Starch-CuOnc

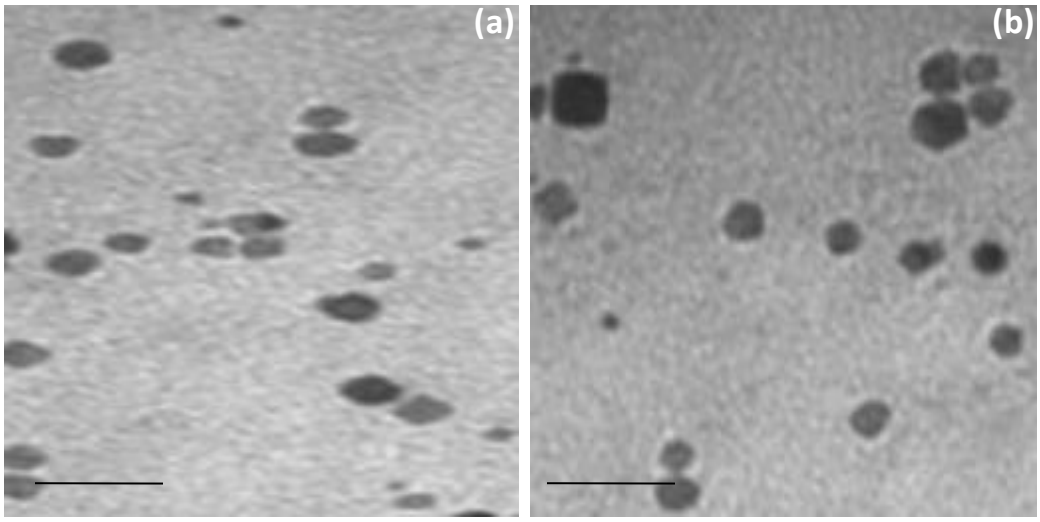

Figure 4: HRTEM photograph of (a) chitosan-CuOnc and (b) Starch-CuOnc

C. Kinetic studies

In Figure 5, typical UV spectra of the drugs are given. The time dependent UV spectra of the drugs during the oxidation reactions catalyzed with CuOncs are presented in Figure 6. The time of completion of the oxidation reaction varies with the chemical nature of the drugs. The absorbance versus time plots for each drug solution with chitosan-CuOnc and starch-CuOnc catalyst is shown in Figure 7. The limiting region in the exponential plots of absorbance versus time indicates the completion of the oxidation as well. It was found that in the presence of H_2O_2 and the catalyst degradations are faster and completed in one hour than those in the absence of catalyst which took nearly 48 hours for completion. The kinetic plots for the rate coefficient determination under pseudo first order conditions which are generated by plotting log ODo/ODt versus time are shown in Figure 8. The first order rate coefficient (k) values are determined from the slope values of the kinetic plots multiplied with 2.303.The best fit linear plots are found for the pseudo first order conditions only. In Table 1, the rate coefficient values (k) and the half life periods of the various drug oxidations studied are presented. In the Table 1, the $t_{1/2}$ values which refer to the time for 50% degradation of the initial concentration of the drug, agree well from the values calculated from the first order rate coefficient value. Adopting similar procedure, the rate coefficient values and the catalyst feed mass, ranging from 0.5mg, 1mg and 1.5mg are determined. Figure 9shows the pH profiles of the degradation of the three drugs. The optimum pH values corresponding to maximum rate coefficient values of each of drugs agree well within the range of the pKa values of the respective drugs. The pKa values reported in literature are given in Table 1.Keeping all other conditions constant, overall trend observed in the oxidative degradation rate constant of the drugs is GE>FU>DH. Also, maintaining the experimental conditions unaltered, the trend among the CuOnc catalysts having chitosan and starch as stabilizers is found to be chitosan-CuOnc > starch-CuOnc.

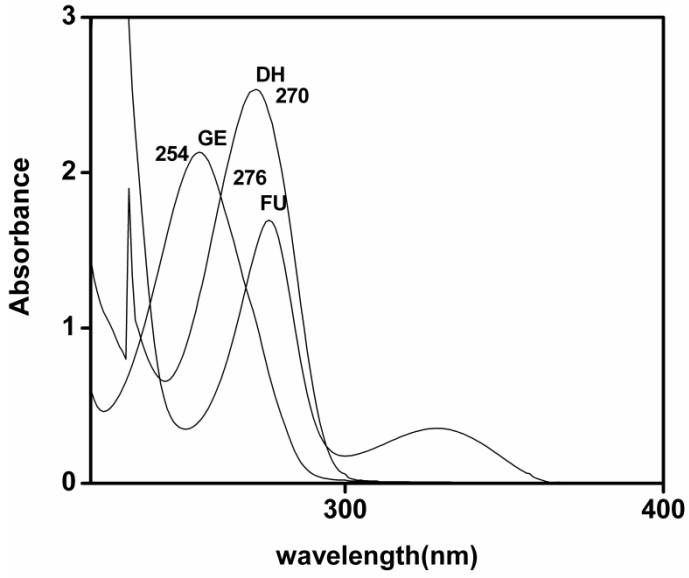

Figure 5: Typical UV spectra of the drugs in water

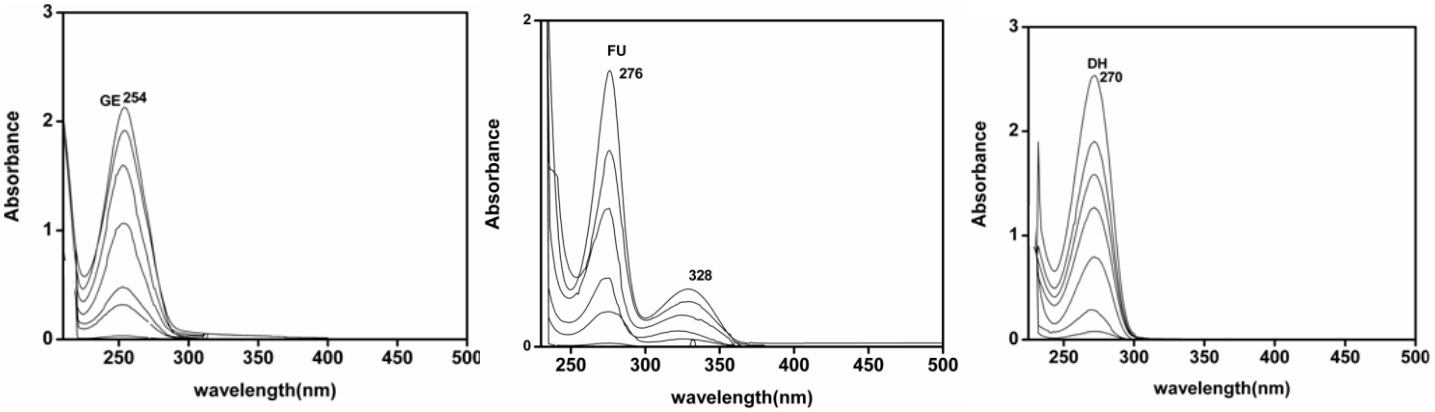

Figure 6: Time dependent UV spectra of the drugs in presence of H_2O_2 and Chitosan-CuOnc at 25^oC

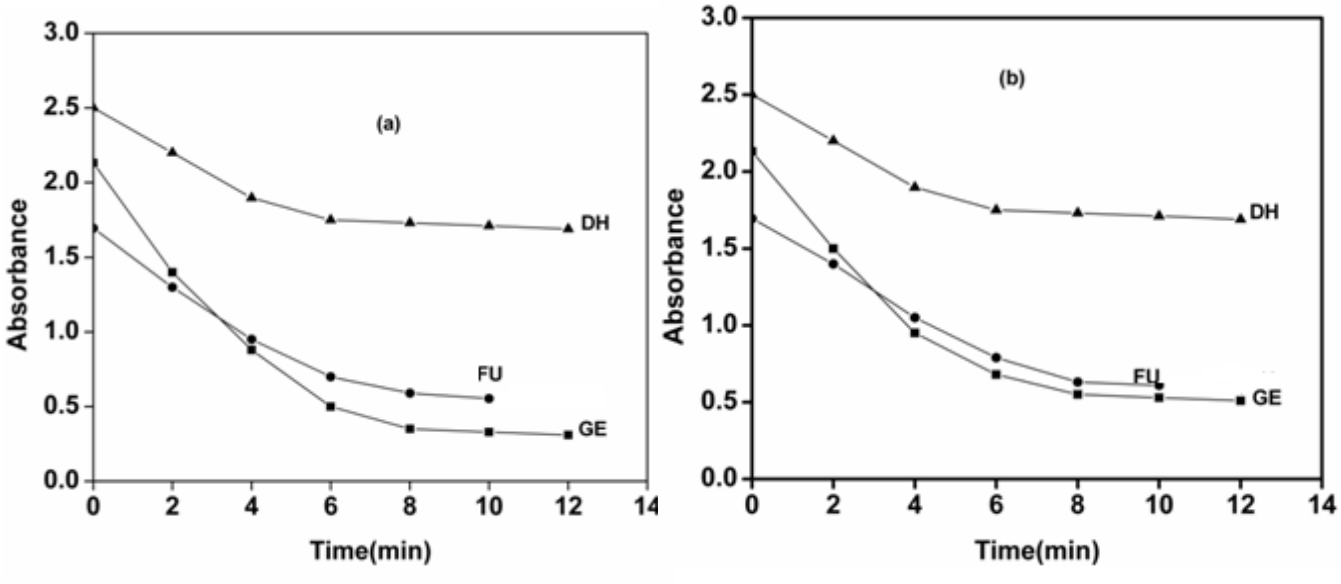

Figure 7: Absorbance versus time plots for the drugs in presence of H_2O_2 and (a) chitosan-CuOnc and (b) starch-CuOnc at 25^oC

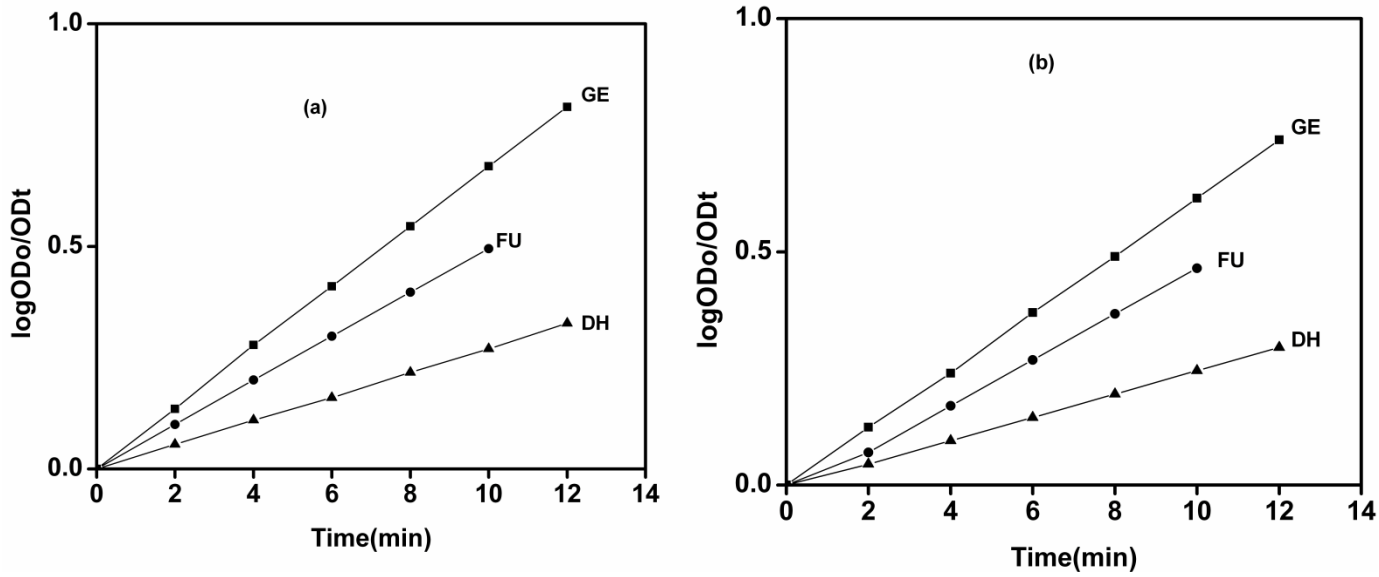

Figure 8: Kinetic plots of log (ODo/ODt) versus time plots of the drugs in presence of H_2O_2 and (a) chitosan-CuOnc and (b) starch-CuOnc at 25^oC

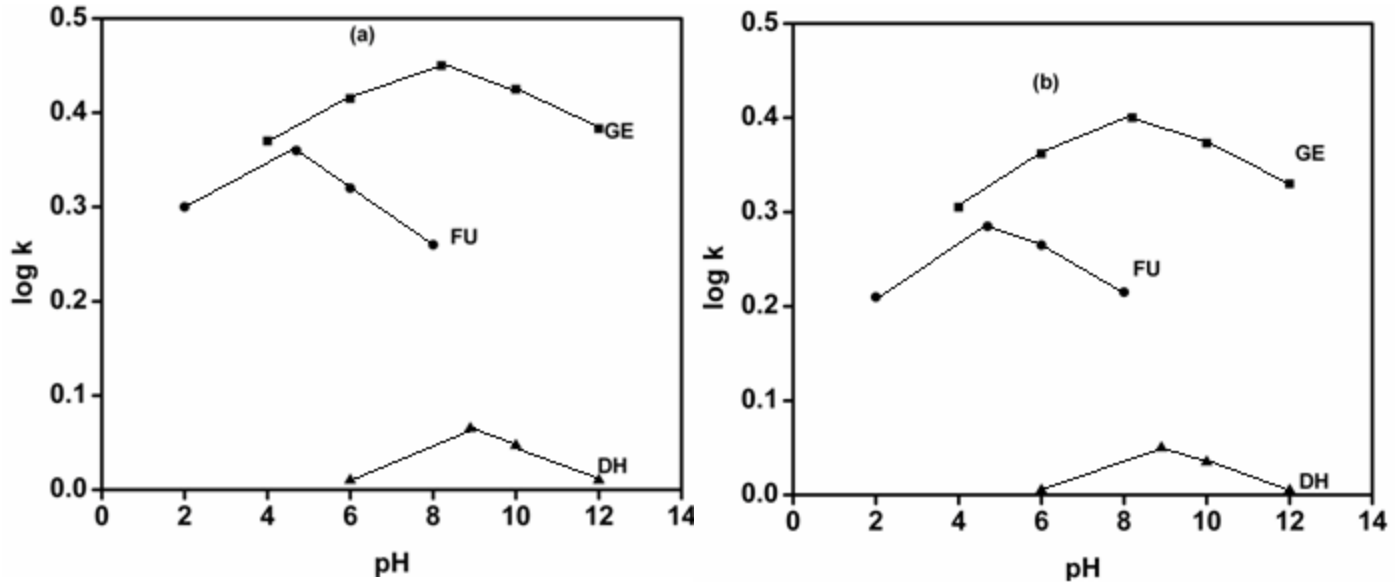

Figure 9: pH profiles of the drugs in presence of H_2O_2 and (a) chitosan-CuOnc and (b) starch-CuOnc at 25°C

Table 1: Pseudo first order rate coefficient (k), half life period $t_{1/2}$, optimum pH of the three drugs determined in presence of H_2O_2 and at starch-CuOnc and chitosan-CuOnc at

DRUG	k(10^{-3}/s)		$t_{1/2}$(10^{2}s)		OPTIMUM pH
	Chitosan – CuOnc	Starch– CuOnc	Chitosan – CuOnc	Starch – CuOnc	
Gentamicin	2.61	2.37	2.66	2.93	8.20
Furosemide	1.90	1.75	3.65	3.96	4.70
Deriphyllin	1.04	1.03	6.66	6.72	9.00

D. Mass effects

For the three drugs chosen in this work the catalyst feed amounts are optimized by studying the catalyst mass effect using 0.5mg, 1mg and 1.5mg of CuOnc separately in each case. The pseudo first order rate coefficient values determined with each of the three catalyst feeds for the drugs using chitosan-CuOnc are given in Table 2. It was found that for all drugs 1mg catalyst feed weight is the optimized catalyst mass which produced the maximum rate coefficient values. The rate coefficient values obtained with 1.5mg catalyst feed are found to be the nearly the same as that found for 1mg catalyst feed. Therefore for all other studies 1mg feed was maintained as the catalyst mass.

In the CuOnc particles stabilized with chitosan, a biopolymer having amine and hydroxyl functional groups, the CuOnc surfaces are surrounded with O atoms of the OH group as well as to some extent N atoms from the amino groups. In the starch-CuOnc the CuOnc surfaces are surrounded with O atom of the OH group of the starch only. Therefore in the acidic pH, chitosan-CuOnc show higher catalytic activity in presence of H_2O_2.

Table 2: Pseudo first order rate coefficient (k) values of GE, FU, and DH for different catalyst starch-CuOnc feeds and chitosan-CuOnc feeds at $25^{O}C$

DRUG	k(10^{-3}/s)		
	0.5mg	1.0mg	1.5mg
Gentamicin	1.25	2.61	2.85
Furosemide	1.05	1.90	2.02
Deriphyllin	0.58	1.04	1.10

IV. CONCLUSION

Among the three drugs investigated in this work, the gentamicin is found to be more efficiently catalysed by CuOnc in presence of H_2O_2 than the rest of the drugs. The biostabilisers such as chitosan, starch was successfully utilized in the preparation of CuOnc in a greener way and the three drugs are mineralized successfully, with chitosan-CuOnc and starch-CuOnc. Chitosan-CuOnc exhibited better catalysis than starch-CuOnc. The optimum pH values for the three drugs are found out and they all seem to lie near the pKa values of the drugs.

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Figures Captions

Figure 1: Molecular structures of the drugs FU:Furosemide, GE:Gentamicin and DH:Deriphyllin
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