# Using A Novel Nano Chitosan-Ampicillin Drug to Study the Effective Range of Drug Level Outside the Affected Cells

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**Abstract**

The work is divided into two parts, the first include synthesis a nano Chitosan-Ampicillin drug, by the esterification reaction between nano Chitosan and Ampicillin drug, as it was characterized via FT-IR, $^1$HNMR, and AFM techniques. The second parts; included, the study of drug release in two acidic values (5.0 and 7.5) at constant temperature 310 K; where the choice of these two values depends on that the pH of the extracellular tumor is in the range of 6.5-7.5, while the endosome and lysosome are 4.5-5.5. The study gave great results, by linking the drug (Ampicillin) with the nano chitosan; because the urgent need to retain the drug within the effective range for longer time, this driving us to look for a new optimization method for drug release.

Keywords: Esterification reaction, Condensation polymerization; Selectivity; Buffer solution; Swelling; Drug delivery system, Ampicillin drug

## 1. Introduction

Linear polysaccharides like chitosan are straight-chain copolymers made up of D-glucosamine and N-acetyl D-glucosamine [1]. This biopolymer is produced by Partial DE acetylation on chitin, which is the most abundant basic biopolymer and has a similar structure to cellulose. Chitosan is found in the cell walls of parasites, yeast, and the exoskeletons of arthropods such as insects, crabs, and shrimp [2]. Chitosan is pH-dependent, non-toxic, anti-bacterial, easily bio absorbable, biodegradable, high molecular weight and biocompatible [3]. Due to its many advantages, it has been used for various vital medical purposes such as wound healing, tissue regeneration, anti-infective activity, antacid and ulcer activity that prevents or weakens drug-induced stomach irritation. Chitosan is known to have immune stimulating effects, antitumor activities, increased protective effects against infections caused by some pathogens, and anticancer activities [4]. Chitosan Nano particals has been used as an anticancer and used as a drug delivery system in the treatment of cancer cells, as it has great potential to overcome some obstacles that prevent effective targeting of cells and molecules in cases of inflammation and cancer [5,6]. The drug delivery system is considered one of the best ways to help the drug reach the target sites, as drug delivery systems refer to being polymeric or lipid-carrying systems that transport drugs to their targets or receptor sites in a manner that provides maximum therapeutic efficacy and prevents its deterioration or disruption during transportation to the site. Target sites) and protect the body from negative reactions [7]. The goal of a drug delivery system is to release the drug to provide maximum safety, efficacy, and reliability simultaneously [8, 9]. Dissolution or biodegradability can be brought in the case of hydrogels approximately via hydrolytic, enzymatic, or environmental (temperature, pH, or electric powered subject) pathways; but, the degradation isn't continuously ideal relying on the time frame and area of the drug transport tool [10]. Hydrogels, with excessive water content material in addition to tissue such as mechanical homes, and are showed being able to combine together with cells for engineer diverse tissues in each vivo and vitro [11].

## 2. Material and Methods

All chemicals were used in this work of analytical grade.

### Synthesis of Nano Chitosan-Ampicillin Drug

Ampicillin drug (9.2 g, 0.03 moles) were dissolved in 30 ml THF with three drops of concentration HCl and added to nano chitosan (4.77g, 0.0005 moles) and

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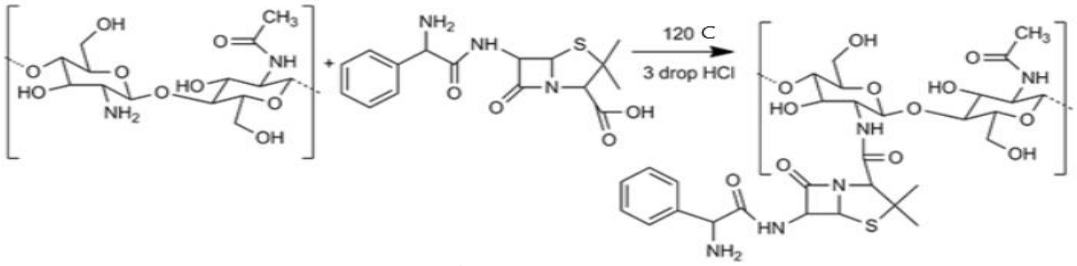
reflex for 24 hr. Finally the precipitate was washed by diethyl ether and 2.0 M NaOH and leave to dry for 16 hr.




*Equation (1): Synthesis of Novel Nano Chitosan- Ampicillin drug*

## Release Ampicillin Drug from Novel Nano Chitosan-Ampicillin drug (13)

The release of drug from the polymeric system in two pH values 5.0 and 7.5, by taking one gram of novel nano Chitosan-Ampicillin drug and immersing it in a beaker containing 50 ml of buffer solution (pH=5.0 and pH=7.5) respectively, and the release is followed up every time (hour and day) by taking a sample of the solution and examining it with an UV-Vis spectrophotometer.

## 3. Results and Discussion

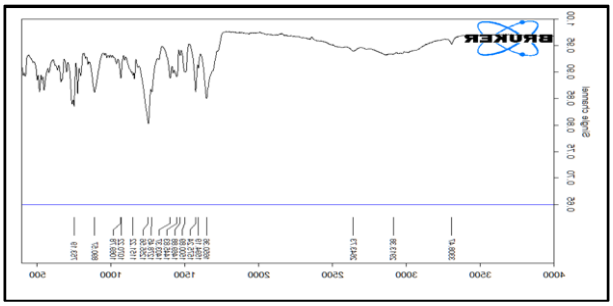


*Figure (1): FT-IR spectrum of novel nano Chitosan-Ampicillin drug*

Figure (2), showed 1H NMR (400 MHz, DMSO-d6) δ

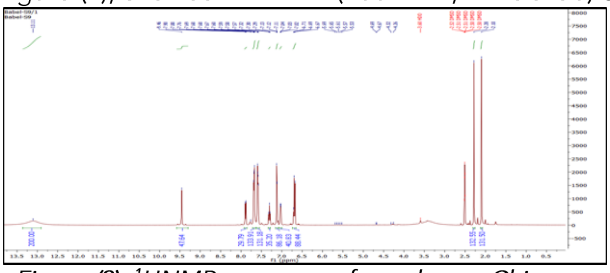


*Figure (2): $^1$HNMR spectrum of novel nano Chitosan-Ampicillin drug*

## Synthesis of Novel Nano Chitosan-Ampicillin drug

The physical properties of synthesis novel nano Chitosan-Ampicillin drug were M.P. 325-327, Yield 77%, Color White-brown and Mobile phase was (Ethanol 3:1 Hexane) and R*f* = 0.78. Figure (1), show the FT-IR (KBr, $cm^{-1}$): ν 2500-3400 (OH), 2973 and 2859 (CH, sp3), 3307 (NH), 3012 (CH, $sp^2$ of aromatic rings), 1501 bend (NH), 1470 (bend of $CH_2$), 1401(bend of $CH_3$), 1647 (polymeric ester, C=O), 1594 (polymeric carboxyl, C=O).

broad singlet peak at 12.32 ppm for the polymeric hydroxyl group, singlet at 8.68 ppm for the drug free primary amine, singlet at 8.27 ppm for the NH of the secondary drug amide, 7.74-7.38 ppm for the protons of the polymeric aromatic benzene, 6.30 and 6.26 ppm for the protons of aromatic drug benzene, The multiplate peaks at 5.58-5.50 ppm to the proton of carbon 14 & 30, 5.19 ppm for the protons of atom 13 & 29, singlet at 4.86 ppm for the protons of atoms 16 & 31, 4.61 ppm for the proton of atom 52 & 75, 3.06 ppm for the proton of 61 & 84, 1.41 ppm for the protons of methyl groups.

## Release Drug from Novel Nano Chitosan-Ampicillin drug

Tables (1, 2) and Figures (3) to (6) are outlining the release of drug from the polymeric system in two pH values 5.0 and 7.5.

The choice of these two acidity values based on, that the pH of tumor extracellular is in the range of 6.5-7.0, whereas the endosome and lysosome are 4.5-5.5.

**Table (1): Release of drug (Ampicillin) per time (hours and days) in pH=5.0 and constant temp. 310k**

| Time (Hours) | Naproxen drug Concentration Absorbance (λ max.) | | | | |
|---|---|---|---|---|---|
| | 0.2 | 0.4 | 0.6 | 0.8 | 1.0 |
| 1 | 0.171 | 0.174 | 0.188 | 0.198 | 0.215 |
| 2 | 0.196 | 0.213 | 0.223 | 0.234 | 0.252 |
| 3 | 0.254 | 0.258 | 0.264 | 0.279 | 0.287 |
| 4 | 0.279 | 0.288 | 0.301 | 0.319 | 0.352 |
| (Days) | | | | | |
| 1 | 0.305 | 0.335 | 0.373 | 0.413 | 0.438 |
| 2 | 0.354 | 0.384 | 0.455 | 0.478 | 0.546 |
| 3 | 0.435 | 0.462 | 0.512 | 0.566 | 0.596 |
| 4 | 0.482 | 0.506 | 0.534 | 0.586 | 0.637 |
| 5 | 0.482 | 0.506 | 0.534 | 0.586 | 0.637 |

| Table (2): Release of drug (Ampicillin) per time (hours and days) in pH=7.5 and constant temp. 310k | | | | | |
|---|---|---|---|---|---|
| Time (Hours) | Naproxen drug Concentration Absorbance (λ max.) | | | | |
| | 0.2 | 0.4 | 0.6 | 0.8 | 1.0 |
| 1 | 0.011 | 0.016 | 0.019 | 0.023 | 0.027 |
| 2 | 0.023 | 0.028 | 0.035 | 0.042 | 0.047 |
| 3 | 0.032 | 0.038 | 0.043 | 0.052 | 0.059 |
| 4 | 0.036 | 0.043 | 0.049 | 0.058 | 0.064 |
| (Days) | | | | | |
| 1 | 0.066 | 0.073 | 0.079 | 0.088 | 0.098 |
| 2 | 0.076 | 0.083 | 0.092 | 0.099 | 0.116 |
| 3 | 0.084 | 0.092 | 0.098 | 0.106 | 0.125 |
| 4 | 0.095 | 0.099 | 0.109 | 0.123 | 0.137 |
| 5 | 0.095 | 0.099 | 0.109 | 0.123 | 0.137 |

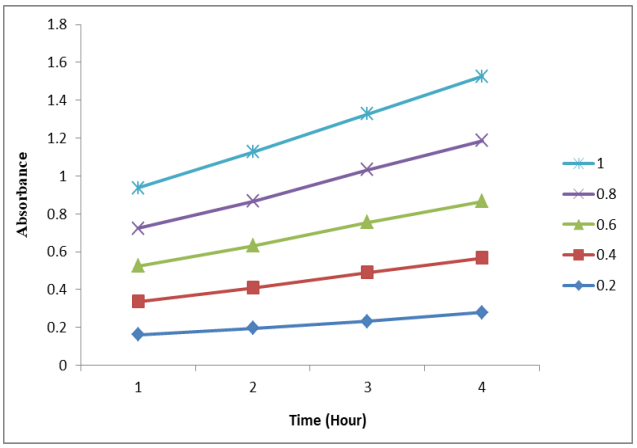



*Figure (3): Release of drug per time (hours) in pH=5.0 at cons. temp. 310k*

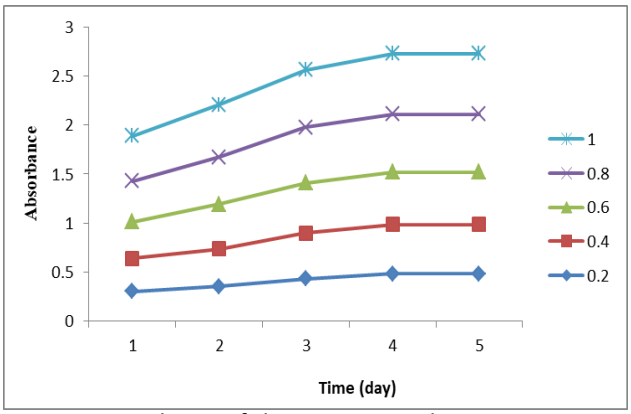



*Figure (4): Release of drug per time (days) in pH=5.0 at cons. temp. 310k*

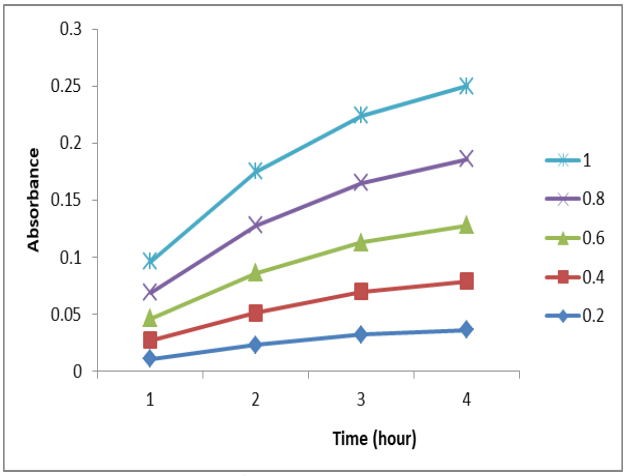



*Figure (5): Release of drug per time (hour) in pH=7.5 at cons. temp. 310k*

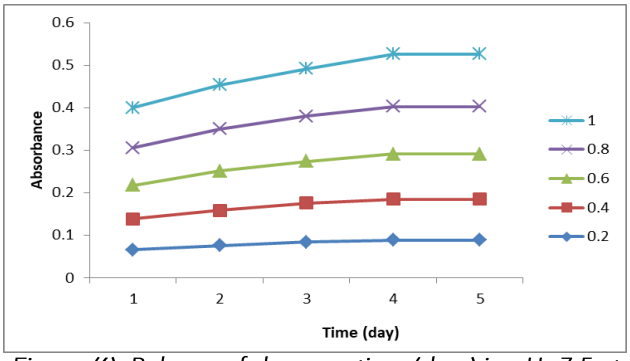



*Figure (6): Release of drug per time (days) in pH=7.5 at cons. temp. 310k*

From the foregoing, it becomes clear to us that with the increase in the concentration of the released drug, the absorbance increases, and the greatest percentage of absorbance was in the acidity function pH=5.0

## 4. Conclusions

The phenomena that lead to transition the drug from its polymeric carrier into its desired site termed as "drug release". When medication is abused, its levels in the human plasma are usually oscillated, in which at the beginning its level is too high then being decreases with time. So the urgent need to retain the drug within the effective range for longer time, this driving as to look for a new optimization method for drug release. The choice of these two acidity values based on, that the pH of tumor extracellular is in the range of 6.5-7, whereas the endosome and lysosome are 4.5-5.5.

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