Synthesis and Physicochemical Characterization of Chitosan-Derived Prodrug Polymers with Antioxidant Activity

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Abstract: Prodrug design is a good way for drug targeting through changing the physiochemical, biopharmaceutical and pharmacokinetics properties, so prodrugs are active chemical agent undergo conversion *in vivo* to release the active drugs. The research apply it's lighting toward an important functional groups to permit the synthesis of prodrug polymers through a chemical reaction between chitosan and succinic anhydride by using suitable conditions (thionyl chloride as drops and 5ml of sulpheric acid (IN)) by way for one hour and at (60 Celsius) the reflux process was done for each amoxicillin and cephalexin as drugs and their detailed molecular structures of both prodrug polymers were characterized by FT-IR, ^{1}H-NMR spectrums. XRD analysis of prodrug polymer P5 appears a sharp peak at (28.07 degree) with high intensity that matched it's crystalline nature of polymer (P6) (607) while thermal analyses (TG, DTG, DTA, DSC), TG curve show's one decomposition stage (35 Celsius) and DTG appears three stages of mass losing at three temperatures degrees (36,50,85 Celsius) while DTA curve clear's three decomposition stages. On the other hand TG curve of prodrug polymer (P6) reflect's two decomposition stages at (50,73 Celsius) DTG curve appears three temperatures (36,70,85 Celsius) and with three weight losing percentage (94.5%, 99.1%, 98.75%), so DTA curve reflects one decomposition stage at (70celsius), DSC thermogram of prodrug polymer reaction at (54.9celsius) as (P5) show's an endothermic compared with the other polymer (P6) to fix same fact of an endothermic reaction at (51celsius), while swelling ratio percentage of prodrug polymer (P6) is (217%) on the time (72 hour) as compared with the other swelling ratio polymer of prodrug (P5) is (197%) at same time (72 hour). Controlled drug release results explain the suitable time (72 hour) to achieve an increasing of controlled drug release at (PH=7.4). For prodrug polymer (P5) as (0.265 nm) as absorbance Lastly, antioxidant activity of prodrug polymer (P5) appears highly DPPH scavenged percent (97.74%) at (2.5mg/ml)as a concentration .

Keywords: Synthesis, Characterization, Amoxicillin, Succinic anhydride, Prodrugs.

1. BACKGROUND

Chitosan is gathered from lineage of natural sources but mostly obtained from Shrimps and krill [1], Summarily there are many routes for industrial production of chitosan such as: demineralization, deporteination, bleaching and deacetylation [2].

Chitosan can be used in medical application based on their Properties: non-toxic and recyclable making it's as biomaterial in the medicine field and in the drug deliver y and a stringent [3, 4] due to finding amine group in the structure that allow's for an inhibition of both gram- positive and gram-negative bacteria [5].

Also natural polymer (Chitosan) can be used as adhesive bandage, absorbent and medical Scaffolds [6]. Chitosan act's one of drug carriers have been improved for nasal, transdermal, oral and intraverous pathways [7].

Both of natural and synthetic polymers take a huge attention in biomedical fields due to their properties: biodegrability, biocompatibility drug/gene, loading capacity [8]. Succinic anhydride is the simplest saturated cyclic anhydride and commonly used for modifying the drug molecule to reach good solubility and pH-responsive of drug release, and succinic anhydride containing hydroxyl or amino groups through esterification reaction [9]. poly anhydride (succinic anhydride) is a useful bioabsorbed material reflect's polymeric matrices in controlled drug delivery System [10].

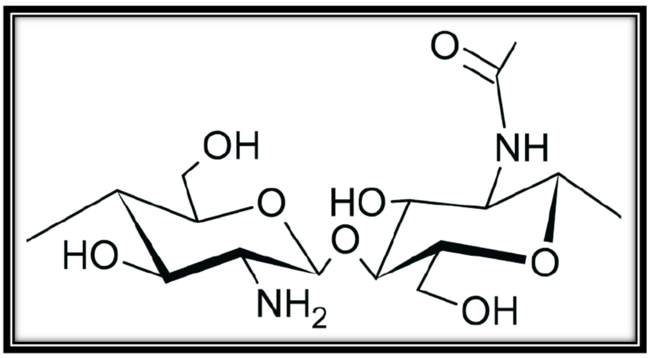

Figure 1: Chemical Structure of Chitosan.

Amoxicillin is a ß-lactam antibiotic against both of gram-positive and gram- negative bacteria. Amoxicillin has two ionizable group and moderate-spectrum in the physiological range, and it has a good bioavailability (95%) taken orally [11].

Cephalexin it is used for treatment respiratory tract infections, skin, soft tissues and bones due to susceptible organisms and cephalexin can be used orally. Cephalexin give's alow activity against gram-negative bacteria while give's high activity against gram-positive [12].

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Table 1: Chemicals and their Purities

Chemicals	Company	Molecular weight	Purity %
A moxicillin	Sammarra	365.4	99.9
Cephalexin	Sammarra	347.39	99
Chitosan	CDH	58	98
Succinic anhydride	CDH	100.07	99.9
Sulpheric acid	Alfa	98	98
Thionyl chloride	Alfa	118.97	98

2. MATERIALS AND TEST METHODS

2.1. Materials

2.2. Testing Methodologies

2.2.1. Infrared Characterization

The apparatus used for infrared spectroscopy characterization is SHIMADZU the acquisition between (4000-400 cm^{-1}) as a wave number range and the number of scans are (15).

2.2.2. Nuclear Magnetic Resonance Characterization

Proton - Nuclear Magnetic Resonance instrument Bruker Biospin GmbH through using DMSO-d6 and the number of scans are (16).

2.2.3. XRD Characterization

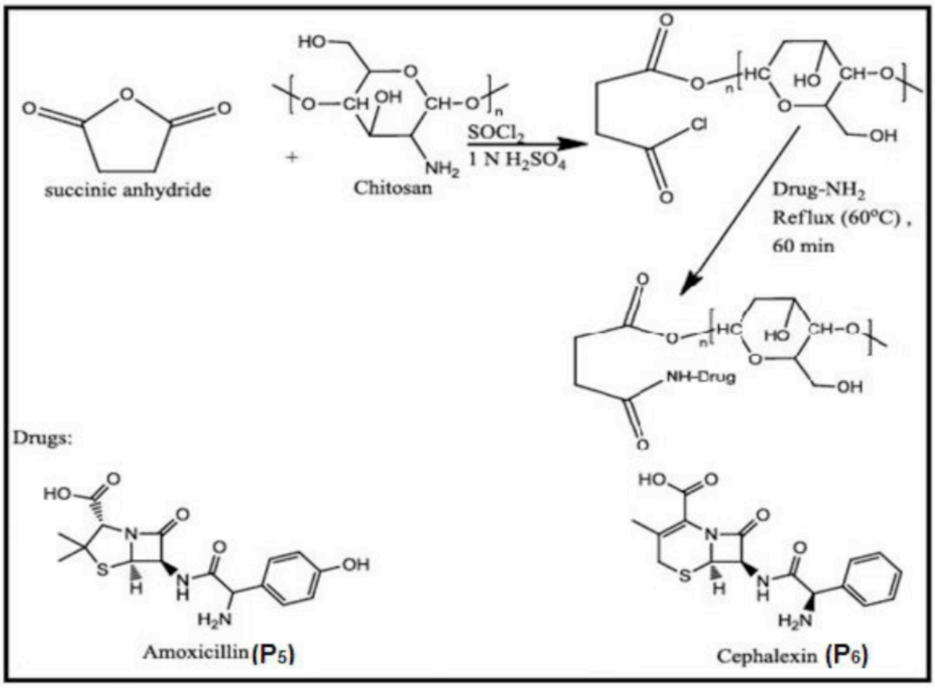
X-ray diffraction is good analysis for studying the Crystalline property of polymers and the spectra was obtained by using (Dr. ben Yamin Instrument co, Ltd, Iran) the scanning rate was (1 sec) all results were obtained by @ 2004 PAN analytical B.V. computer program.

2.2.4. Thermogravimetric and Differential Scanning Calorimetric Characterization

Differential thermal analysis techniques were used (TG, DTA, DTG) for both prodrug polymers (P5, P6) through multi tasking software controlling the various modules (2 mg) of the sample was taken and the temperature range (20-90)C° ,and only differential scanning calorimetry (DSC) analysis was carried through NETZSCH proteus software as an instrument

2.2.5. Swelling Ratio of Polymers

The swelling ratio of both polymers (P5, P6) were characterized by using UV-visible spectrophotometer (200-700 nm) and through ostwald viscometer to carry viscosity of polymers at (37C°) in distilled water.



Scheme 1: Synthesis of prodrug polymers (P_5, P_6).

2.2.6. Controlled Drug Release

Drug release results of polymers (P_3, P5) were done by using UV-Visible spectrophotometer at (37C°) as temperature degree exact buffer solution with (PH= 7.4).

2.2.7. Antioxidant of Polymers

The whole idea of this application is using of (DPPH) radical scavenging of different concentrations of each polymer sample (0.1562, 0.3125, 0.625, 1.25, 2.5) mg/ml and incubated on the plates for 24 hour, and after this reaction DPPH violet color convert's into Yellow Color as reflection of positive result of this application.

2.2. Method

2.2.1. Synthesis of Chitosan – Drugs Conjugates

Put in a beaker (1gm) of succinic anhydride dissolved in (25 ml) of acetone and (1gm) of chitosan dissolution in (25 ml) a solution including both of (glacial acetic acid that diluted in distilled water) after that period of time the addition of (5 ml) of (IN) H_2SO_4 [13] as portions and (3drops) of thionyl chloride was rounded out and the refluxing of the mixture go ahead for one hour and the heating at (60 C°) on the hotplate with (4000 rpms) as rotation speed, then the addition of (0.5 gm) of each amoxicillin, cephalexin was carried separately for mixture and the reflux process was repeated at same conditions. The filteration of products was done firstly, then washing of products for many times by using a suitable organic solvent (diethyl ether). lastly, leaving these products for drying in a room temperature.

3. RESULTS AND DISCUSSION

3.1. Spectroscopic Characterization

Through FT-IR spectrum significant functional groups were appear as shown in the Table (**2**) and the Figure (**4**) for both polymers (P5, P6) [14].

Table 2: Important Functional Groups of Polymers (P5, P6)

Prodrug polymer	Frequencies cm^{-1}	Functional groups
P_5	3437	(N-H) amine
	3057	(C-H) aromatic
	2885	(C-H) alkane
	1703	(C=O) ester
	1633	(C=O) amide
	1583	Asymmetric Str(N-O)
	1556	Asymmetric Str(N-O)
	1465 1427	(C=C) aromatic
	1338	Asymmetric Str(N-O)
	1259	(C-N) amine
	1219-1155	C-O
P_6	3057	(N-H) amine
	2906	(C-H) aromatic
	2791	(C-H) alkane
	1703	(C=O) ester
	1633	(C=O) amide
	1469 1429	(C=C) aromatic
	1259-1219	(C-N)

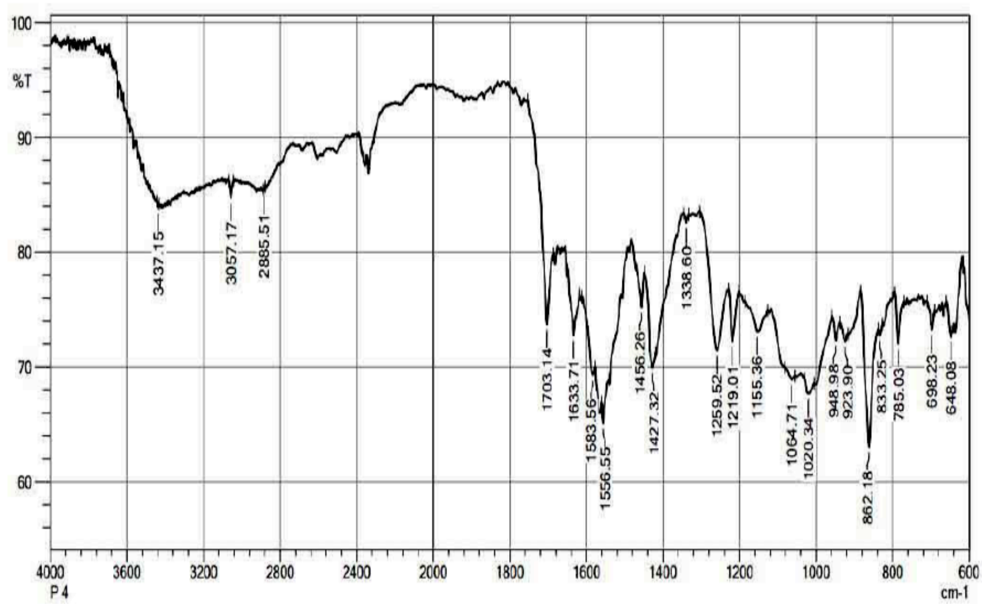


Figure 2: FT-IR Spectrum of Prodrug Polymer (P_5).

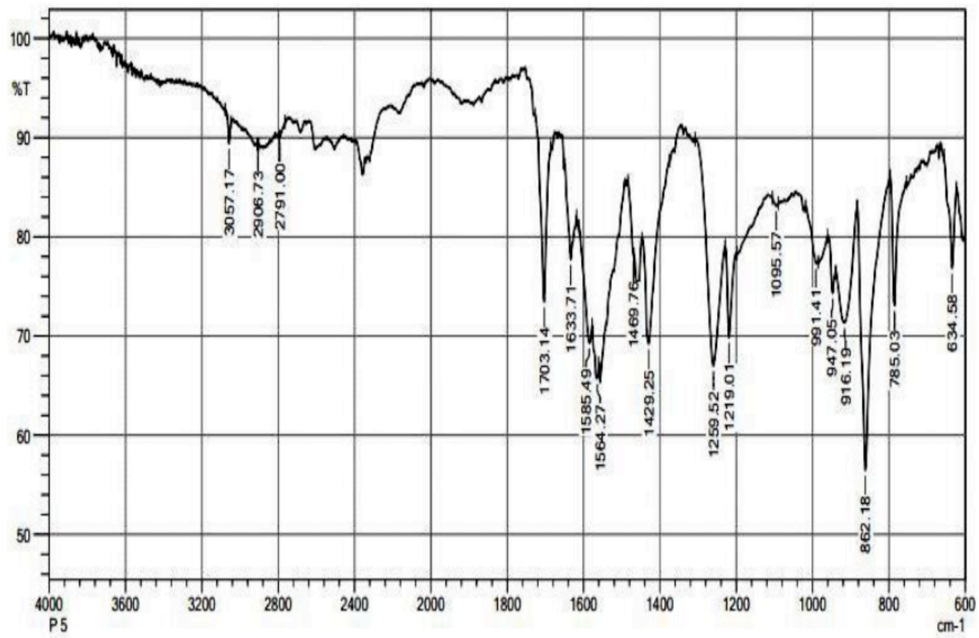


Figure 3: FT-IR Spectrum of Prodrug Polymer (P_6).

While [1]H- NMR of polymers (P_5, P_6) results [15] were listed in the Table as shown in the Figure (**6**):

Table 3: [1]H- NMR of Prodrug Polymer (P_5)

Prodrug Polymer	Chemical Shift (ppm)	Type of Proton
P_5	1.38-1.91	CH3
	2.09 2.84	CH2-CH2-C=O
	3.62	(H N - CH - COOH)
	4.73-5.27	CH=CH-C=O
	6.28-7.52	CH=CH-C=O
	8.20-8.63	proton of aromatic
	9.22	proton of =O carboxylic acid C-OH

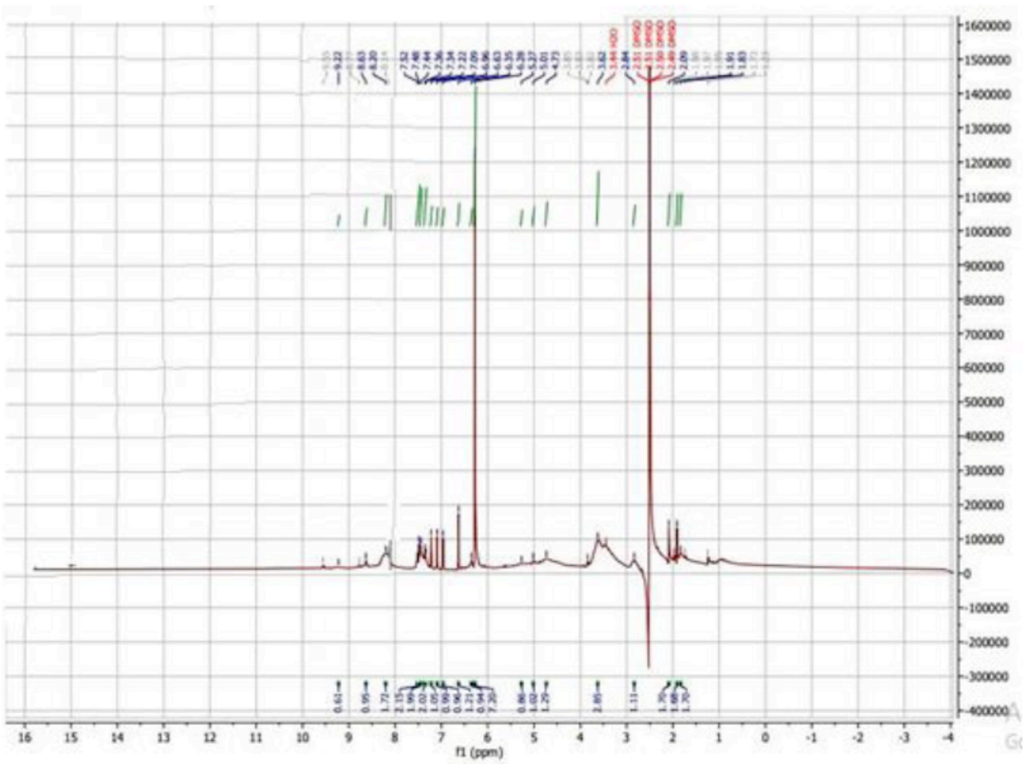


Figure 4: [1]H-NMR of Prodrug Polymer (P_5).

Table 4: [1]**H-NMR of Prodrug Polymer (P6)**

Prodrug Polymer	Chemical Shift (ppm)	Type of Proton
P_6	1.83-1.98	proton of CH3
	2.09	proton of CH2 2.86
	4.52 -4.74	(C - CH – C=O)
	6.63	HC=CH
	7.34 -8.20	proton of aromatic
	9.27	proton of =O carboxylic acid C-OH

3.2. XRD Characterization

The XRD analysis of polymers (P_5, P_6) explained as sharp peaks(2θ) of the diffraction angle at 17.69 degree, 22.88 degree and 28.07 degree with peak intensities of 96, 148 and 607 correspondingly it's crystalline nature of polymer (P_5) [16] according to the Figure (**8**) as in the Table (**5**)

Table 5: XRD of Prodrug Polymer (P_5)

Pos. [°2Th.]	Height [cts]
17.69(1)	96(15)
17.74(1)	48(15)
22.88(3)	148(6)
22.94(3)	74(6)
28.071(4)	607(20)
28.142(4)	303(20)

While prodrug polymer (P_6) show's these diffraction peaks (2θ): 15.22 deg., 17.55 deg., 22.50 deg, 28.05 deg, 32.21 deg, 33.32 deg. 38.28 deg, 39.42 deg., 40.55 deg., 51.3 deg. 57.95 deg. and 58.11 degree as shown in the Figure (**9**) as in the Table (**6**).

Table 6: XRD of Prodrug Polymer (P6)

Pos. [°2Th.]	Height [cts]
15.22(6)	18(5)
15.26(6)	9(5)
17.553(3)	371(13)
17.597(3)	186(13)
22.502(4)	387(15)
22.559(4)	194(15)
28.053(1)	1963(40)
28.124(1)	981(40)
32.216(9)	122(14)
32.298(9)	61(14)
33.32(1)	116(17)
33.40(1)	58(17)
38.285(7)	198(19)
38.384(7)	99(19)
39.42(1)	79(12)
39.52(1)	39(12)
40.55(2)	37(7)
40.65(2)	18(7)
51.3(1)	6(5)
51.4(1)	3(5)
57.95(2)	61(12)
58.11(2)	30(12)

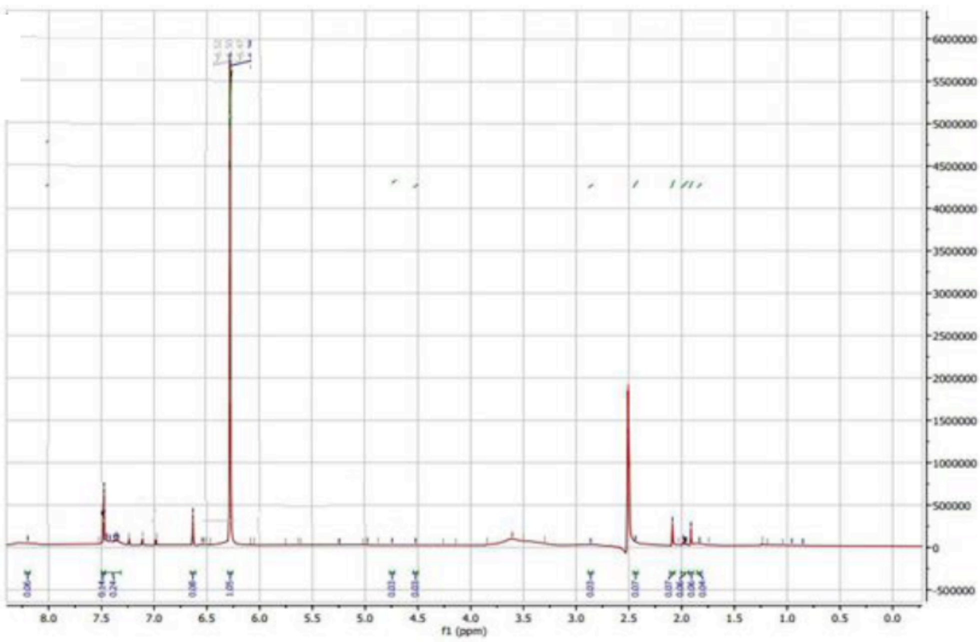


Figure 5: [1]H-NMR of prodrug polymer (P6).

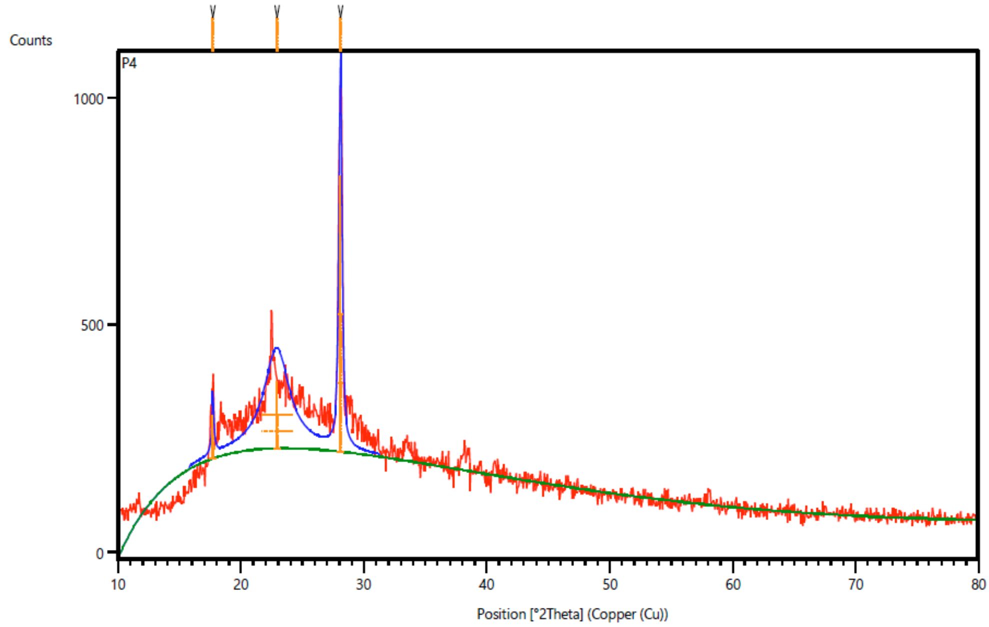


Figure 6: XRD of Prodrug Polymer (P5).

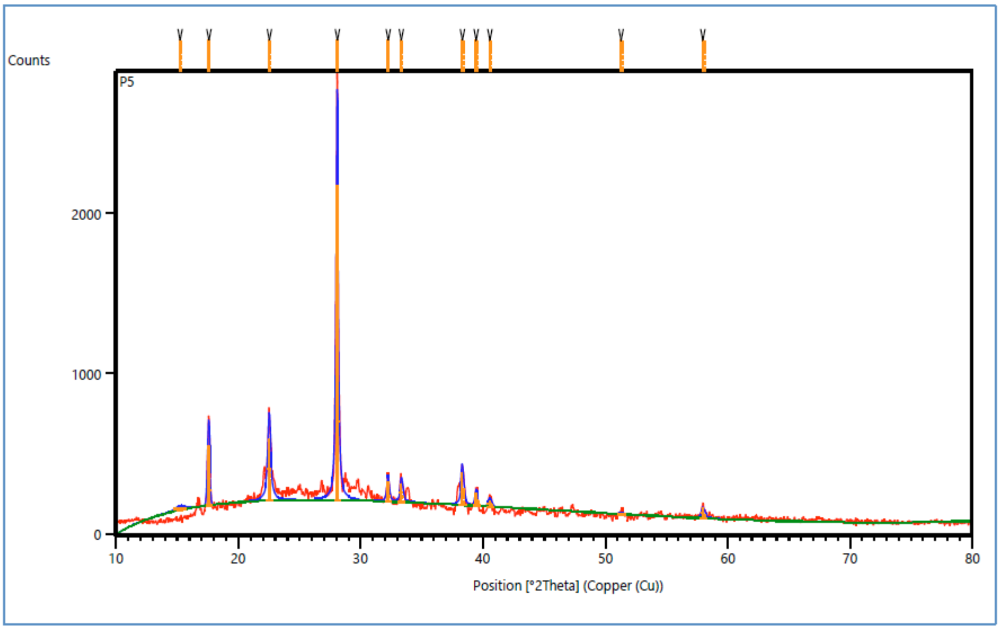


Figure 7: XRD of Prodrug polymer (P6).

All these peaks indicated to low Crystallinity degree and by that the nature of polymer (P5) is amphorous than polymer (P6) [17].

3.3. Thermogravimetric Analysis and Differential Scanning calorimetry

TG Curve regard's a finger print of tested polymers and different chemical and biological substances. Thermogravimetric curve (TG) Show's the thermal decomposition at (35 C°) through one stage, While DTG Curve there are three stages of mass loss occured in three temperature degrees (36,50,85 C°) with different weight losing percentages. So for DTA Curve there are three decomposition stage [18].

TG Curve of Polymer (P6) is represented by two decomposition stages at (50, 73 C°) with (99.85%. and 99.3%) and DTG curve of same polymer is explained by three decomposition stages (36, 70, 85 C°) and weight loss (94.5%, 99.1, 98.75%), while DTA Curve reflect's one decomposition at (70 C°) [19]. Differential scanning calorimetry (DSC) of Prodrug polymer (P5), can be clear at (54.9 C°) with two endothermic Peaks according to the Figure (**10**), Both melting peaks indicated to low Crystallinity which makes this polymer flexible and tensile and the thermal analysis of prodrug polymer (P6) appear's the main endothermic peak set (51 C°) [20] as shown in the Figure (**11**).

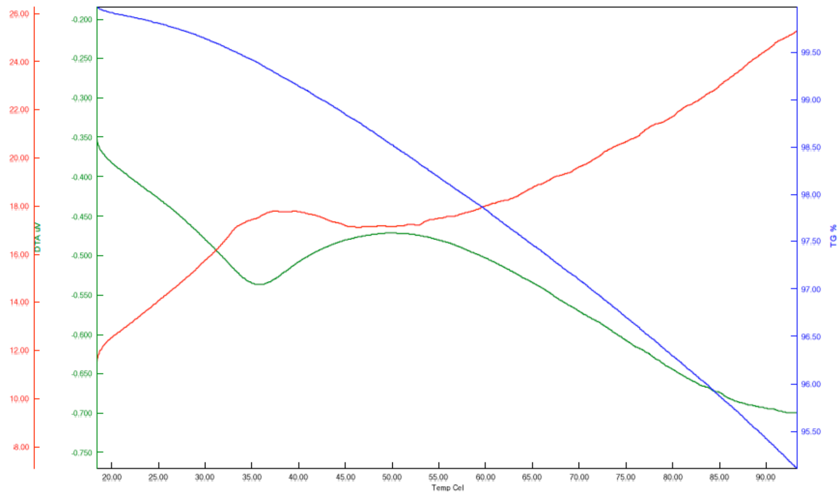


Figure 8: Thermal Analyses (TG, DTA DTG) of Prodrug Polymer (P_5).

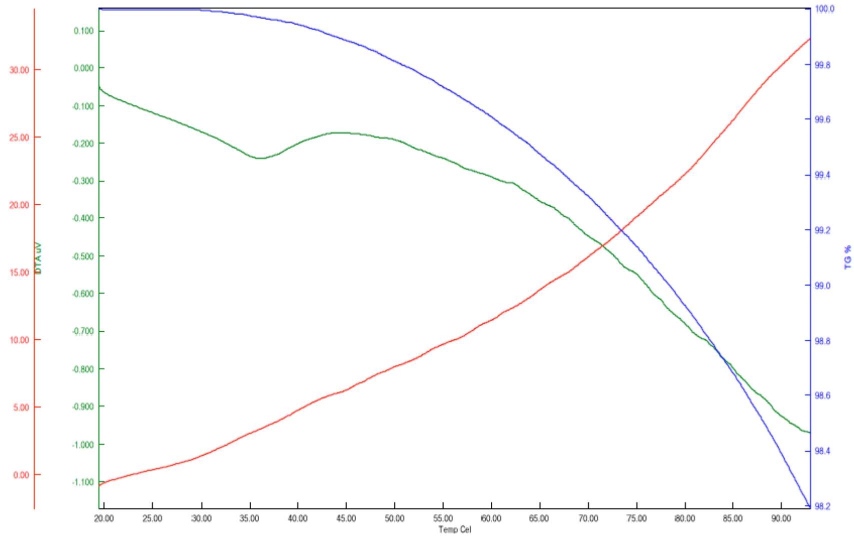


Figure 9: Different Thermal Analysis Curves of Prodrug Polymers (P_6).

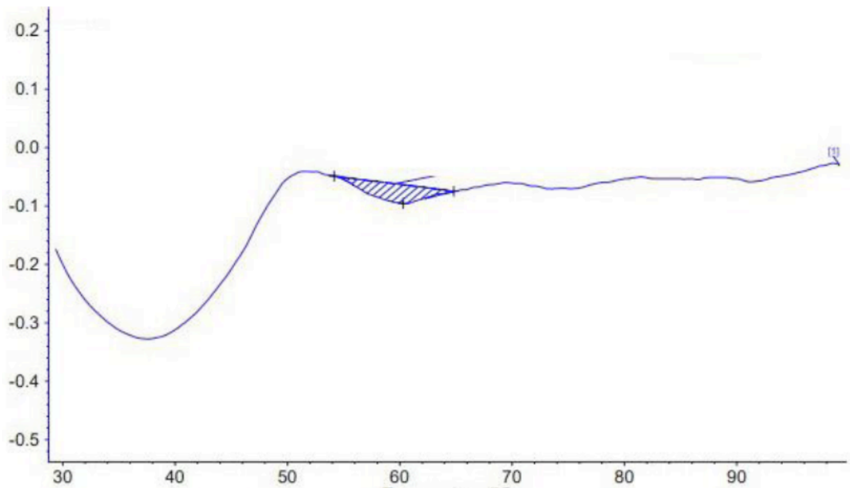


Figure 10: DSC Thermogram of Prodrug (P5).

3.4. Swelling Ratio of Polymers

Dynamic swelling was carried by gravimetric measurements of Organic Polymer hydrogels (P_5, P_6) were putted in a good solvent water as an ideal solvent [21] and these results were listed in the Table (**6**) and shown as in the Figure (**12**).

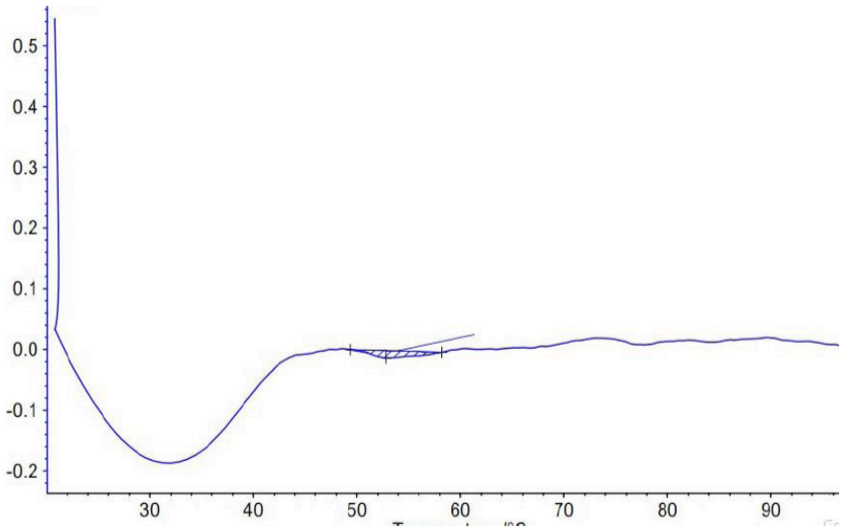


Figure 11: DSC thermogram of prodrug (P6).

Table 7: Swelling Ratio of Polymers (P_5, P_6)

Time (hours)	Swelling ratio% (P_5)	Swelling ratio% (P_6)
24h	89.33333333	120.1666667
48h	126.3333333	195.6666667
72h	197.1666667	217.1666667

3.5. Controlled Drug Release of Polymers

Controlled release is an attainable and good characteristic for drug delivery systems. In some cases, drugs containing nucleophile groups can cause an increasing chain length of the polymer and so increasing of the rate of drug expulsions polymer molecular weight, drug distribution, polymer blending and crystallinity [22].

From the results of prodrug polymer (P_5), controlled drug release is more greater than (P_6) as another prodrug polymer due to different reasons: molecular weight, drug absorption, drug diffusion and the swelling ratio of each polymer [23].

3.6. Antioxidant Application of Polymers

Antioxidants play a crucial role for the protection of human body against any damage occurred by reactive oxygen species. General antioxidant properties of chitin and it's derivatives against free radicals such as; diphenyl-picryl- hydrazy (DPPH), hydroxyl, superoxide, and peroxide were studied with time as based on the de acetylation and the concentration of the polymer. Primary amino groups of chitosan structure through it's reaction with free radicals to form (NH_3) groups

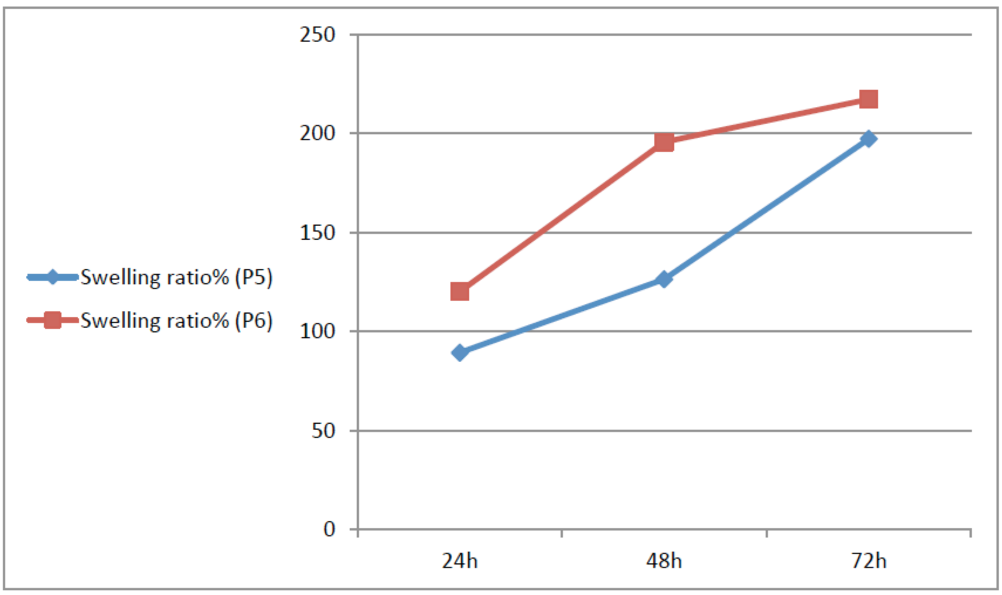


Figure 12: Swelling ratio of Polymers (P_5, P_6).

Table 8: Controlled Drug Release of Prodrug Polymer (P_5) at PH =7.4

Time (hours)	Abs (nm)	Abs (nm)	Abs (nm)	Average
1h	0.175	0.177	0.181	0.177667
2h	0.201	0.0.213	0.198	0.1995
6h	0.219	0.219	0.226	0.221333
12h	0.226	0.231	0.238	0.231667
24h	0.239	0.241	0.248	0.242667
48h	0.248	0.251	0.255	0.251333
72h	0.244	0.265	0.258	0.255667

Table 9: Controlled Drug Release of Prodrug Polymer (P_6) at PH=7.4

Time (hours)	Abs (nm)	Abs (nm)	Abs (nm)	Average
1h	0.097	0.082	0.077	0.085333
2h	0.95	0.098	0.11	0.101
6h	0.119	0.123	0.119	0.120333
12h	0.128	0.13	0.133	0.130333
24h	0.131	0.137	0.135	0.134333
48h	0.13	0.139	0.14	0.136333
72h	0.141	0.138	0.147	0.142

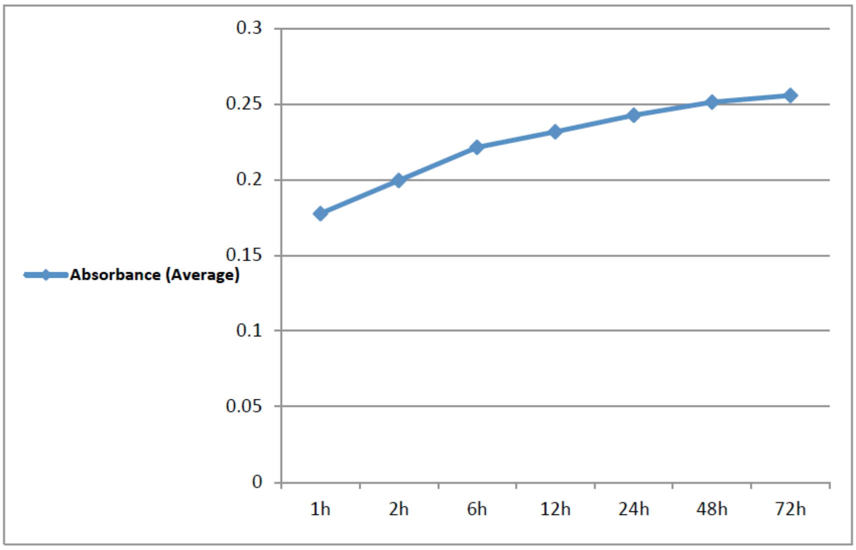


Figure 13: Controlled Drug Release of Prodrug Polymer (P_5) at PH =7.4.

Table 10: Antioxidant Activity of Prodrug Polymer (P_5)

Concentration (mg/ml)	Abs(nm)	Abs(nm)	Abs(nm)	DPPH scavenging (%) (P_5)
0	0.151	0.139	0.153	0
0.15625	0.015	0.019	0.017	88.48758465
0.3125	0.028	0.009	0.012	93.00225734
0.625	0.01	0.006	0.007	95.93679458
1.25	0.004	0.005	0.004	97.06546275
2.5	0.003	0.004	0.003	97.74266366

chitosan exhibit's antioxidant properties and by that regard's as a natural antioxidant due to it's small value of molecular weight [24].

CONCLUSION

Drug carriers are generally effective vehicles for preserving drug molecules due to their controlled

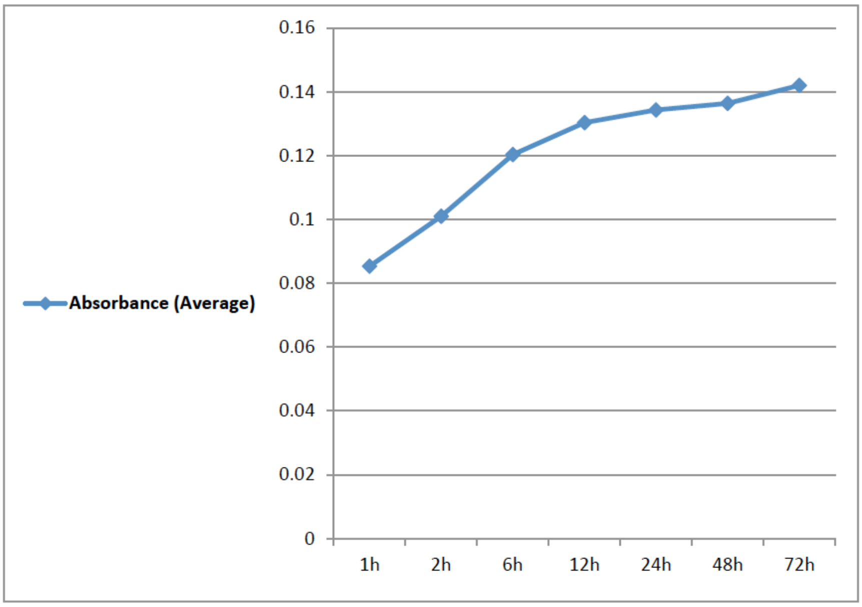


Figure 14: Controlled Drug Release of Prodrug Polymer (P_6) at PH =7.4.

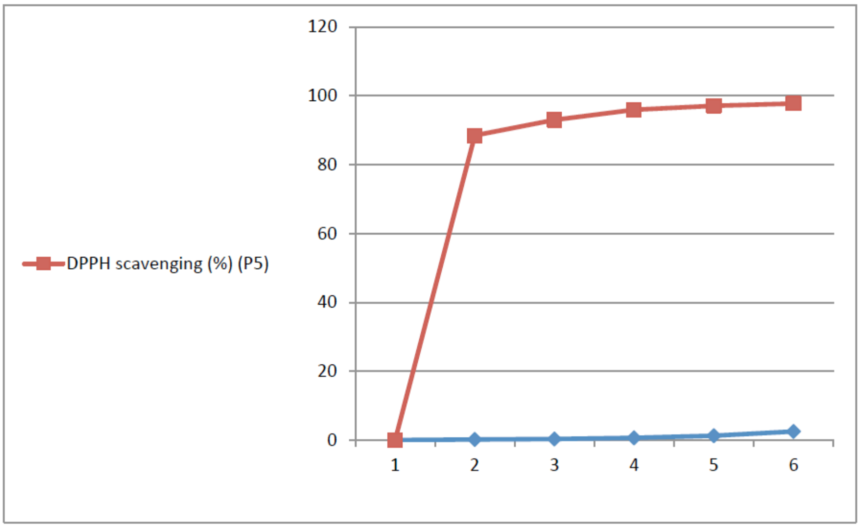


Figure 15: Antioxidant Activity of Prodrug Polymer (P5).

Table 11: Antioxidant Activity of Prodrug Polymer (P6)

Concentration (mg/ml)	Abs(nm)	Abs(nm)	Abs(nm)	DPPH scavenging (%) (P_6)
0	0.151	0.139	0.153	0
0.15625	0.02	0.023	0.021	85.5530474
0.3125	0.012	0.014	0.017	90.29345372
0.625	0.007	0.009	0.009	94.35665914
1.25	0.005	0.006	0.005	96.38826185
2.5	0.003	0.003	0.004	97.74266366

release behavior. Based on the results of all analyses, significant observations indicate a low degree of crystallinity. Thermal analysis of these polymers suggests that the reactions are endothermic, which contributes to improved polymer flexibility and tensile properties.

The controlled drug release from polymer (P5) is greater than that from polymer (P6). This difference may be attributed to several factors, including drug diffusion, swelling ratio, and the molecular weight of the polymer. Furthermore, chitosan can be regarded as a

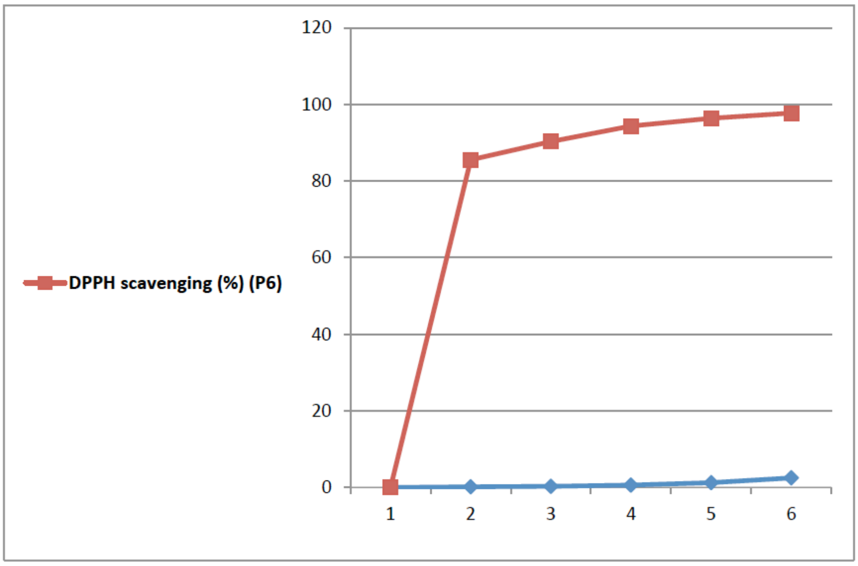


Figure 16: Antioxidant activity of prodrug polymers (P6).

natural antioxidant, which is associated with its relatively low molecular weight.

CONFLICTS OF INTEREST

The author declared no conflicts of interest.

REFERENCES

[1] Alessandro pellis, Georgm Guebitz and Gibson Stephen Nyanhongo "Chitosan: Source, Processing and Modification Techniques", Gels, (2022); 8: 393, p: 1. https://doi.org/10.3390/gels8070393

[2] Riyona Desvy Pratiwi, Sjai Khurrizal E / Muttaqien Nuhik, Najla Salsabilla Difa, Gita Syahputra and A'liyatur RosYidala, "Eco-friendly Synthesis of Chitosan and it's Medical Application from Chitin Extraction to Nano particle Preparation, ADMET Journal, (2023), 11 (4), 438. https://doi.org/10.5599/admet.1999

[3] Rindudo M, "Chitosan in Medicine Properties and Applications" Prog polymer Sci, (2006), (31) p: 603-632. https://doi.org/10.1016/j.progpolymsci.2006.06.001

[4] Kumar, M. N. V.R "A, review of Chitin and Chitosan Applications, React. Funct. polymer (2000), (46), P: 1-27. https://doi.org/10.1016/S1381-5148(00)00038-9

[5] Andres Giraud. L, Gerente. C, Le. Cloriec, p., "Antibacterial Effects of Chitosan Powder: Mechanisms of Action, Environ. Technol. (2007), (28), P: 1357-1363. https://doi.org/10.1080/09593332808618893

[6] Fatemeh Asghari, Mohmmad Samiei, Khor Sro Adibkia, Abolfazl Akbar Zadeh and Soodabeh Davaran, "Biodegradable and Biocompatible Polymers for Tissue Engineering Application: a review, (2017), Volume (45), issue (2), P: 192. https://doi.org/10.3109/21691401.2016.1146731

[7] Parhi, R, "Drug Delivery Applications of Chitin and Chitosan: A review, "Environ. Chem. Lett, (2020), (18), P: 577-594. https://doi.org/10.1007/s10311-020-00963-5

[8] Ning Ding, "Homogenous Etherification Modification of High-Strength Hydrogel", Journal of Physics, (2022), p: 2263.

[9] Pulikanti Guruprasad Reddy and Abraham J. Domb, "Poly anhydride chemistry", Biomacromolecules Journal, (2022), (23), p. 4954. https://doi.org/10.1021/acs.biomac.2c01180

[10] Yu Xin Wan, Zhenze Xie, Mingjie Wang, Yuelian Liu, Mubin Zheng, Dong Xu and, "Esterase-triggered rapid release of succinic anhydride conjugated curcumin co-prodrug for osteosarcoma therapy", European Polymer Journal, (2023), Volume (198), 112382, P: 2. https://doi.org/10.1016/j.eurpolymj.2023.112382

[11] Samareshghosh, "Recent Research and development in Synthetic polymer -based drug delivery systems", Journal of Chemical Research, (2004), P: 243. https://doi.org/10.3184/0308234041209158

[12] Rafik Karaman, Samia Alkurd, Reem Yaghmour, Ahmed Amro and Dons a Karaman "Antibacterial activity of novel prodrug of Amoxicillin and Cephalexin", world Journal of pharmaceutical Research, (2015) volume (4)), Issue (9), p: 12.

[13] Rafik Karaman, Samia Alkurd, Reem Yaghmour , Ahmed Amro and Dons a Karaman " Autibacterial activity of novel prodrug of amoxicillin and cephalexin" world Journal of pharmaceutical Research, (2015) volume (4)), Issue (9), p: 12.

[14] Gan B- Bajracharya, Rashmi Koju, etal, "plasticizers Synthesis of Phthalate esters Via $FeCl_3$ Catalyzed nucleophilic addition alcohols to phathalic anhydride", Results in chemistry, volume (3), p: 1. https://doi.org/10.1016/j.rechem.2021.100190

[15] Ammar A. Ali Beg and Ahlam J. Qasir, "Synthesis and Antimicrobial Study of possible Mutual prodrugs of Amoxicillin and Metronidazole by direct and Indirect coupling through spacer", Iraqi J. Pharm Sci, (2014), vol 23 (1), p.5.

[16] Rama Muruga Pandian, Simona Clement and Vijayalak Shmi Uthriapathy, "Fabrication and *in vitro* Drug Delivery Evaluation of Cephalexin Monohydrate loaded PLA: PVA/HAP: TiO2 Fibrous Scaffolds for Bone Regeneration", American Chemical Society, (2023), Vol: 8, P: 5021. https://doi.org/10.1021/acsomega.2c07701

[17] Talla Shruti, Wadher Kamlesh, Umekar Milind and Loni ya R.T, "Formulation, Optimizing and Evaluation of solid Dispersion of Deferasirox using Factorial Design", Journal of Drug Delivery and Therapeutics (2024), 14 (5), P: 29. https://doi.org/10.22270/jddt.v14i5.6526

[18] Alina Mustatea, Roxana Trusca, Bogdan Trica and Donia Dimonie," XRD studies of the Morphological changes generated by interface Agents for obtaining New scalable sustainable Sustainable Blends Based on starch and PCL", chem. proc., (2023), 13(4), P: 3. https://doi.org/10.3390/chemproc2023013004

[19] Pawel Ramos, "Application of Thermal Analysis to Evaluate Pharmaceutical Preparations Containing Theophylline", pharmaceuticals, (2022), (15), 1268, p.3. https://doi.org/10.3390/ph15101268

[20] Adriana Fulias, Gabriela Vlase and Titus Vlase etal, "Comparative Kinetic analysis on Thermal Degradation of

some Cephalosporins using TG, DSC data", Chemistry Central Journal, (2013), 7: 70, P: 1. https://doi.org/10.1186/1752-153X-7-70

[21] Jennifer Bourgeois, Laure- Anne pierson, Julien Nicolas Muriel Lalanne, Patrick Couvreur and Karine Andrieux, "Application of Thermal Analysis to the Study of lipidic prodrug Incorporation into Nano Carriers ", J. Chem Anal calorim, (2009), (98), p. 68. https://doi.org/10.1007/s10973-009-0350-7

[22] Dhuha R. Kashash, Mohanad M. Kareem and Naser A. Naser, "New N-substituted Maleimide Drug polymers, Synthesis, Drug Release and Antibacterial Activity," "Egypt. Acad. J. Biolog. Sci, (2024), 16(1), p. 66. https://doi.org/10.21608/eajbsc.2024.336266

[23] S. Freiberg, X, Zhu, "Polymer Microspheres for Controlled Drug Release", International Journal of Pharmaceutics, (2004), (282), p.5. https://doi.org/10.1016/j.ijpharm.2004.04.013

[24] Luminita Georgeta Confederat, Cristina Gabriela Tuchilus, Maria Dragan, Mousa Sha'at, and Oana Maria Dragostin, "Preparation and Antimicrobial Activity of Chitosan and it's Derivatives, A concise Review", Molecules, (2021), 26, 3694, P: 12. https://doi.org/10.3390/molecules26123694

https://doi.org/10.12974/2311-8717.2026.14.02