Starch Sulfonation and Substitution with Amoxilline and Folic acid

Shurooq S. Kadhim
Al-Mustansiria University
College of Science, Department of Chemistry

Abstract

Starch was sulfonated and substituted by Amoxilline and folic acid as natural drug polymer . Starch derivatives were characterized using FT.IR and UV spectroscopies.

The synthesis and behavior of bioactive polymeric systems have attracted great interest in this work because the drug is lined to the polymer back – bone via a degradable chemical bond and it is slowly released under appropriate condition.

The intrinsic viscosities were calculated using Ostwald viscometer at 30°C. The controlled drug release was studies in different pH values. Thermal analysis was recorded and physical properties were measured.

Key words : Starch ,Sulfonation , Drugs

Introduction

Starch is a natural polymer, an abundant polysaccharides and low cost carbohydrate that have been used extensively in industry(1,2).

Both synthetic polymers and natural polymers that contain hydrolytically or enzymatically labile bonds or groups are degradable. The advantages of synthetic polymers are obvious, including predictable properties, batch – to – batch uniformity and can be tailored easily [3]. Among the natural polymers, starch is regenerated from carbon dioxide and water by photosynthesis in plants[4]. Owing to its complete biodegradability, low cost and renewability [5,6], starch is considered as promising candidate for developing sustainable materials[7,8].

Many researchers have studies the graft copolymerization onto the starch with vinyl monomers initiated by ceric salts, due to the latter can form efficient redox system in presence of organic reductants[9-10].

Starch can be easily transformed into an anionic polysaccharide, via chemical functionalization [11]. For instance, a carboxylic derivative of starch , maleic starch half-ester, acid (MSA), has been prepared via the esterification of starch with maleic anhydride in the presence of pyridine [12,13]. Applications of starch – based biodegradable polymer include reducing the food losses[14].

Materials and Methods

Starch was supplied by BDH. Chlorosulfonic acid was purchased from Fluka , Amoxilline and Folic acid were obtained from college of pharmacy.

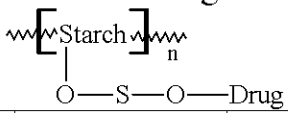
Sulfonation of starch

(5 g,0.03mole) of supplied starch was solubilized in 10ml of dry dioxane to obtain high liquidity, the excess of chlorosulfonic acid (2.5ml) was added gradually with continuous stirring to ensure maximum homogeneity at 0°C about 1day. The reaction mixture was heated at 40°C for 1hr. The solvent was evaporated under vacuum, the viscous resulting modified polymer was obtained then washed and dried in a vacuum oven with 70% yield.

Substitution of sulfonated starch

A mixture of sulfonated starch (2g,0.01mole) and 10ml of dioxane and (0.03mole) of some drugs such as Amoxilline or folic acid were added to reactions mixture, heated at 50°C about 30min. by using water bath the solvent was evaporated the colored modified polymers were obtained, washed with ether and dried at 50°C. The physical properties were listed in Table(1):

Table 1: Physical properties of modified drug starch sulfonated P_2,P_3



No.	Starch	S.P°C	Color	μin dL/g	UV. Absorption λ_{max} nm
P_2	Amoxilline sulfonate	118-125	Brown	0.21	250,330
P_3	Folic sulfonate	180-190	brown	0.25	250,290

Controlled drug release

100mg of prepared drug polymer such as P_2 or P_3 were kept in a cylinder containing 100ml of buffer solution on pH1.1 or 7.4 at 37°C. A sample was analyzed at suitable λ_{max} to determined weight% of release sample by periodically with drawn for several times.

Characterization

Fourier transition infrared (FT.IR) spectra were recorded on a Perkin – Elmer spectrum. Thermal analysis was performing using TGA instruments Φ10 differential scanning calorimeter equipped with a RCS accessory under nitrogen atmosphere.

The sample (5mg) was heated at 400°C at rate 20°C.min^{-1} to record the melting temperatures. UV. Spectra were recorded using shimadzu (UV-vis)-160.

Quantitative analysis corresponding to the amount of pendant sulfonic acid groups in corporated on to starch were remained unreacted was performed by a titration methods as follows:

0.1g of modification polymer P_2 or P_3 was dissolved in 5ml of ethanol the solution was titrated to a phenyl phthalein end point using Sodium hydroxide (0.01M) in methanol. Results were expressed as the content of sulfonic acid groups which were defined as the mole percentage of the starch units. The sample P_1 without modification was also titrated yielding the blank value. The 10% mole was obtained referred to content of starch $-SO_3H$ groups by titration analysis.

Results and Discussion

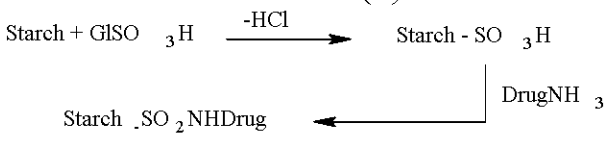
To aid in the structural elucidation of the modified starch with $-SO_3H$ moieties along the backbone was analyzed using FT.IR spectroscopies and assignments for the characteristic groups were developed.

FT.IR spectra of P_2 with contained of remained $-SO_3H$ groups . The absorption at 11376-1177cm^{-1}assignment for SO_2 a symmetric and symmetric (Fig 1).

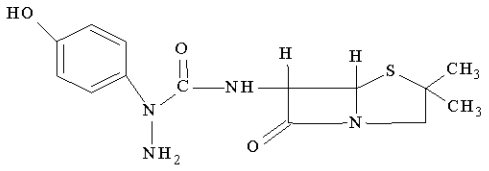
The other peaks were observed at 3450cm^{-1} due to the OH of starch which is remained unreacted and at 3210cm^{-1} due to the NH- sulfonamide, the absorption at 3025cm^{-1} due to CH aromatic of phenyl ring of Amoxilline the remained absorption of C=O caprolactam was observed at 1735cm^{-1} and other C=O of carboxylic acid of Amoxilline was revealed at 1689cm^{-1}.

Modified starch drug sulfonate of Folic acid shows the absorptions of –OH carboxylic acid was observed at 3400-2820cm^{-1} as a broad band, this assignment for folic acid. The absorption was revealed and at 1370-1169cm^{-1} due to SO_2. The absorption at 3250cm^{-1} was attributed to NH sulfonamide (Fig 2).

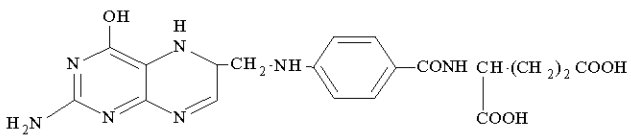
Sulfonation of starch as a natural polymer by using chlorosulfonic acid was carried out at 0°C as shown in Scheme(1).



Drug = Amoxilline , Folic acid



Amoxilline



Folic acid

Thermal analysis

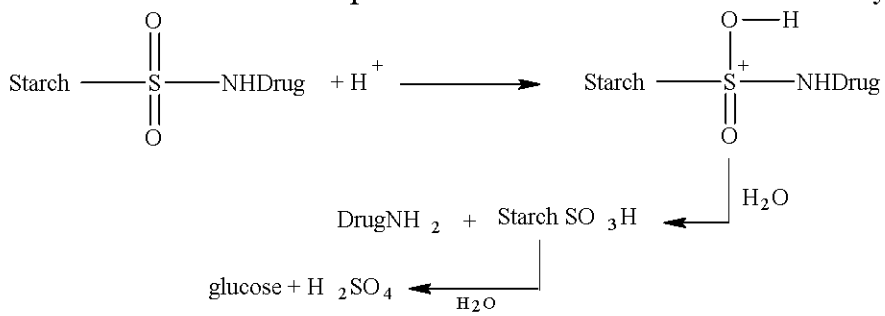
In attempt to understand the thermal behavior of modification starch was investigation by TGA which indicated the thermoplastic behavior ranged the between 118-125°C for P_2,and 180-190°C for P_3 this indicated the thermal plastic behavior which attributed to bonded attachment of amoxilline or folic acid through the backbone of the chains polymers.

In vitro controlled drug release studies

UV. Spectra of prepared drug polymer were recorded for several times for every sample in pH1.1 or 7.4 at 37°C indicated the minimize the absorption intensity of specific λ_{max} which equal to 360nm of pH1.1 and λ_{max} =280nm for pH7.4. The respectively analysis were recorded as (Figs 3 and 4).

This new prepared drug starch sulfonamide group release in acidic medium than basic medium which could predict the ability to be used in stomach hydrolysis as acidic medium.

The suggested mechanism was explained as shown in the followed hydrolysis:



Scheme (2)

The researchers concluded that the incorporation of sulfonamide groups could increase the drug activities, in spite of the parent drug, also the controlled drug release which enhanced the prelong time of the delivery system and the product of the drug-polymer is starch as natural polymer without any toxicity.

The high swelling % was observed in water which attributed to presence of unmodified sulfonic acid groups which could enhance the solubility.

The researchers concluded from this research that the prepared modified starch could be used in stomach as specific cite as acidic medium which could hydrolysis gradually with slow rate as drug carrier polymer, to minimized the side effect of drug and to prelong time of the drug and for other inflammatory drugs which could be usus.

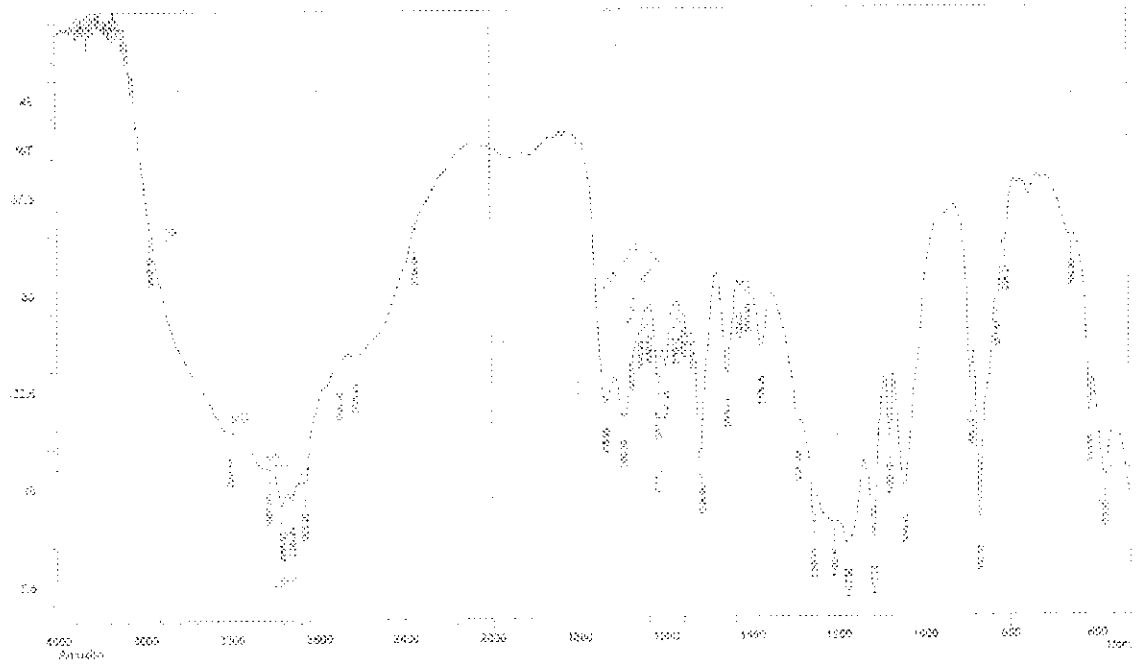


Fig.(1) Amoxilline – starch sulfonamide P_2

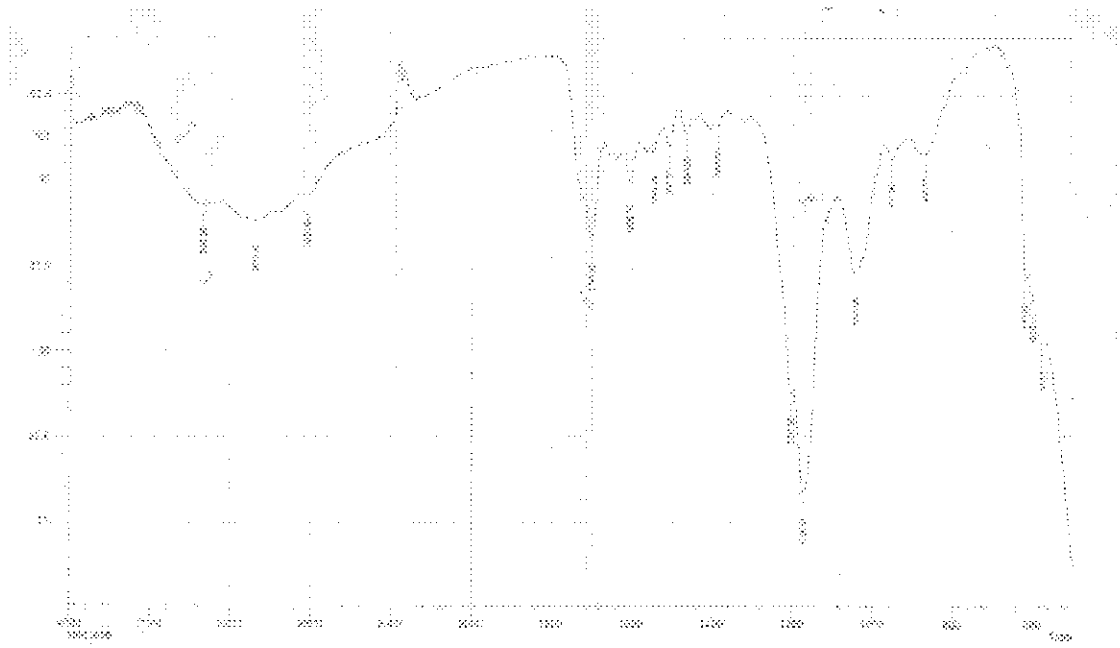


Fig.(2) Starch-Folic sulfonamide P_3

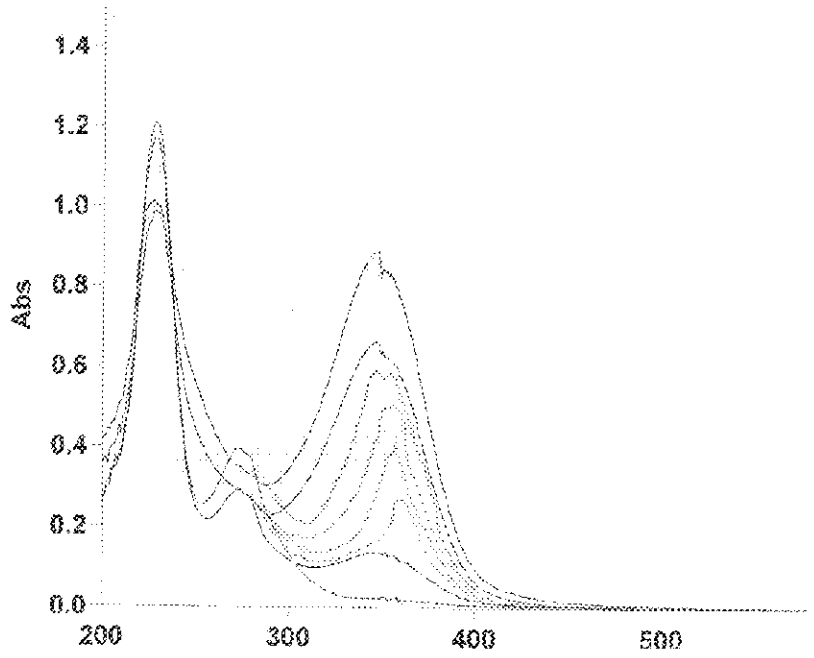


Fig.(3) UV. spectra of P_2 Amoxilline starch sulfonamide at pH1.1

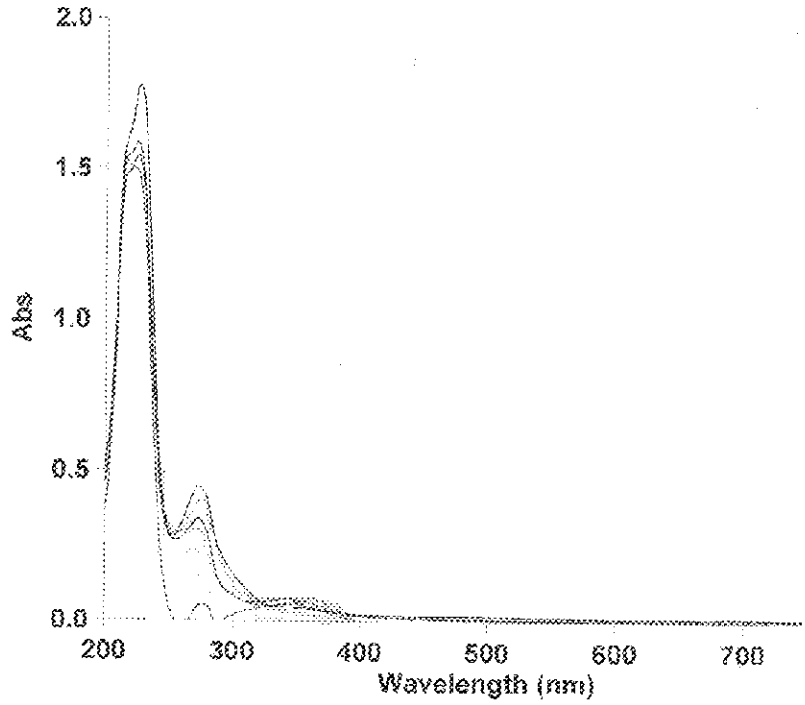


Fig.(4):Folic – starch sulfonamide P_3 at pH7.4

References

1. Mostafa,Kh.M.,Samerkandy,A.R. and El-Sanaby,A.A.2007"Modification of carbohydrate polymers" J. of Applied Sci. Res. 3(8):681-689.
2. Lu,D.R.,Xiao,C.M. and Xu,S.J. 2009"Starch-based completely biodegra - dable polymer mateials" ,EPRESS polym. Letters 3(6):366-375.
3. Nair,L.S.,Laurencin,C.T.2007,Biodegradable polymers as biomaterials. Progress in polymer Sc.,32,762-768.
4. Teramoto,N.Motoyama,T.,Yosomiya,R.,Shibata,M.,2003"Synthesis ,thermal properties and biodegradability of propyl esterified starch, European Polym. J.,39:255-261.
5. Mostafa, Kh. M. and Morsy M.S.,2004"Tailering a new sizing agent for cotton textiles, J. of Applied Sci. Res. 1:335-340.
6. Zhang,J.F.,Sun,X.Z.,2004"Mechanical properties of anhydride, Biomicromolecules,5,1446-1451.
7. Griffin, G.J., Starch polymer blends polymer degradation and stability ,45,241-247.
8. Pareta,R.,Edirisinghe,M..J.2006"A novel method for the preparation of starch films and coating carbohydrate polymer, 63,425-431.
9. Liu, M.Z., Cheng, R.S., and Wu, J.J. 1993.Graft copolymerization of methyl acrylate on to potato starch initiated by ceric ammonium nitrate. Journal of polymer Science , Pa AA,31,318-3186.
10. Song, H. and Ma,X.C.,2003"Synthesis of strong anionic flocculent by grafting starch with acrylonitrile and subsequent treatments. Specialty petrochemicals, 20, 30-33.
11. Crote C.Lazik W.,Heinze T.,2003"Tartaric acid starch ether, A novel biopolymer based polyelectrolyte, Macromolecular Rapid Communication ,24,927-93.
12. Xiao C.M., Ye J.2005,Preparation of the carboxylic anhydride Chines Journal of applied Chemistry 22,643-646.
13. Xiao C.M. Fang F.2009.Ionic self-assembly and characterization of poly saccharide-based poly electrolyte complex of maleic starch half ester acid with chitosan. Journal of Applied polymer Science 112,2255-2260.
14. Zhao R.X., Torley P.,Hally P.J.2008 Emerging biodegradable materials, starch and protein – based bio-nanocomposite materials. Journal of Material Science,43,3058-307.

سلفنة النشا وتعويضه بالاموكسلين وحامض الفوليك

شروق صباح كاظم
الجامعة المستنصرية كلية العلوم قسم الكيمياء

الخلاصة

تمت سلفنة النشا وتعويضه بالاموكسلين وحامض الفوليك كبوليمرات دوائية معوضـــه ، شخصت باستخدام الاشعة تحت الحمراء والاشعة فوق البنفسجية . ان تحضير بـــوليمرات فعالة بايولوجياً من الانجازات المثيرة للاهتمام بسبب ادخال وحدات دوائية ضمن الهيكـــل الرئيسي للسلسلة البوليمرية والتي تساعد على حصول تحلل من خـــلال الأواصـــر التـــي تساعد على التحرر الدوائي تدريجياً تحت ظروف مناسبة . قيست اللزوجـــة الجوهريـــة بدرجة 30°م ، ودرست سرع التحرر الدوائي المحكم بدوال حامضية مختلفـــة . ســـجلت التحاليل الحرارية للبوليمر المحضر ، وقيست الخواص الفيزيائية للبوليمرات المحضرة .

الكلمات المفتاحية : نشا ، سلفنة ، ادوية