March-April 2020
ISSN: 0193-4120 Page No. 11107 - 11115

Poly Ethylene Glycol/Chitosan/Iodine Bio-Composites and Their Applications

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Abstract:
Films were manufacturedfrom poly ethylene glycol /chitosan polymeric matrix with the addition of Iodine for treating wounds infected with the disease, especially diabetes. Iodine element was added with different weight percents (6,8 and 10). As a solution and film states are used to investigate is healing action. Evaluating the healing action is done by applied these solution and films to the injured rat's and the celavix treatment was used for comparing. The antibacterial activity was checked by expose the prepared samples to the action of Escherichia coli (gram negative) and Staphylococcus aureus (gram positive) microorganisms. Agar well diffusion method was used to evaluate the antibacterial action by measuring the inhibition zone diameter.Results showed that I2have the antibacterial ability against both Escherichia coli and Staphylococcus aureus microorganisms and this ability increased with increased I2 content in both films and solutions states. Complete healing obtains within seven days. UV and FTIR results proved presence of physical interaction between PEG-chitosan and iodine and the UV parameter will change with I2 content. Density, wettability, the color degree increased with iodine content.Surface morphologies of the prepared films, it can be concluded the Iodine ability to change the surface topography due to its ability to diffuse among the chains and fill its voids. This conclusion enhanced also by many changes occurred in the roughness parameters,(such as average surface roughness (Sa), core roughness depth (Sk), core fluid retention (Sci) and surface bearing index (sbi)), FESEM image, AFM 3D images, optical microscope images and contacts angles values.From the thermal transition view point, chitosan-PEG blend show miscible blend with single Tg and Iodine acts as plasticizer agent through reduction of Tg from (60.2 to 58.9 ºC).

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I. INTRODUCTION

Poly (ethylene glycol) ; PEG is a poly ether compound , named also polyethylene oxide (PEO) or poly oxyethylene . PEG is a white, waxlike chemical that resembles paraffin. PEG is solid at room temperature, and melts at 104° F. It consists of ethylene glycol/ethylene oxide (-O-CH2-CH2-) repeat units [1]. It possesses high structural flexibility, extremely low immunogenicity, and nontoxicity [2] . Moreover, PEG exhibits excellent pharmacokinetic and biodistribution behavior [3] . Depending on the number of repeat units, the molecular weight of PEG varies from 200 Dalton to 20 kDalton.The polymer is usually linear at molecular weights under 10 kDalton , but branching of PEG occurs at higher molecular weights. In general, lowmolecular-weight PEG (200–800 Dalton) is a liquid, whereas highmolecular-weight PEG (>1 kDalton) is a waxy solid [4] . Both low and high-molecular-weight PEG have a wide range of

March-April 2020
ISSN: 0193-4120 Page No. 11107 - 11115

applications in medical [5, 6] ,chemical [7] , and biological areas [8]. Low molecular-weight PEG is used as a solvent in oral liquids and soft capsules in pharmaceutical products. PEG with higher molecular weights (1–5 kDalton) is often used for the conjugation of proteins, drugs, and oligonucleotides [9] , or other nanocarriers, such as liposomes [10] ,polymeric nanoparticles [11] , or carbon nanotubes [12, 13].The process of surface adsorption, covalent attachment, or entrapment of the PEG molecules toward bioactive drugs, nanoparticles, or polymers is called PEGylation [14] .

PEGylation is widely used in drug delivery, targeting, and vaccination,mainly to achieve high concentrations of PEGylated drugs in aqueous solution (without causing their aggregation), to lower their cytotoxicity and immunogenicity, and to prolong their circulation time [7, 11] .

II. EXPERIMENTAL PART

2.1 Materials Used

Polyethylene glycol (PEG) used as biopolymer provided from Verdean house, Daryaganj, New Delhi-110002 (India) with the properties maintain in(table 1).

Table 1: Properties of the used polyethylene glycol

Propriety	Data
Chemical formula	$[H(OCH_2CH_2)\ OH]_n$
Color	White crystalline flakes
Molecular weight	6000 g/mol
pH	4.0 - 7.0

Chitosan is provided from Shanghai SoyoungBioteah.Inc.Shanghai 201208 (china) with the properties maintain in(table 2).

Table 2: Properties of the used Chitosan

Propriety	Data
Chemical formula	$C_2H_{11}NO_4X_2$
Deacetylationdegree	≥ 90.0%
Particale size	80 mesh
Color	Off white powder

Iodine (I2) was purchased from Flucku, a Swiss company with the following properties (table3).

Table (3): Properties of the used iodine

Propriety	Data
Color	Dark-gray/purple-black
Physical state	Solid element
Density	4.93 $g.cm^{-3}$ at 20°C
Melting point	114 °C
'Boiling point	'184 °C

2.2 Film Formation

The preperd films composed of PEG ,Chitosan and different iodine percent's (6,8,10 wt%) as shown in table 4. Chitosan dissolve in 2% aqueous acetic acid with high stirring until completely dissolved , then poured in petri dish (Bees waxed to help in releasing the film), then leaved to air dryness .The formed film covered on iodine particle for coating by sublimation process (transfer of iodine crystal to nano vapor molecules deposit on the film , as shows in figure (1).

Figure 1. PEG /Chitosan /I2 film (A) 6% I2 (B) 8%I2 (C) 10%I2

Table (4) Weights and percent's of the films formed for three samples

March-April 2020
ISSN: 0193-4120 Page No. 11107 - 11115

Sample No.	PEG		Chitosan		I_2	
	g	%	g	%	g	%
1	0.20	26.6	0.49	65.4	0.06	8
2	0.20	26.6	0.47	62.8	0.08	10.6
3	0.20	26.6	0.45	60	0.10	13.4

2.3 Tests

To Determinate of antibacterial activity, Muller Hinton agar plates (Agar Well Diffusion Method) were prepared and inoculated with test organisms (Escherichia coli , staphylococcus aureus)by spreading the inoculums on the surface of the media with the help of sterile swab. [15]. FTIR test was carried out using (IRAFFINITY-1) (Shimatzu) to check the structure of polymer. The spectral absorption of iodine solution is done by UV-Vis double beam spectrophotometers, (SHIMADZU, UV-1800, Japan) . All spectra were measured at room- temperature in a quartz cell with a 1 cm optical path length. Wettability test achieved by using SL 200C - Optical Dynamic I Static Interfacial Tensiometer& Contact Angle Meter which manufactured in KINO Industry Co., Ltd., USA with contact angle range from 0° to 180°.

III. RESULTS AND DISCUSSION

3.1 Anti bacterialaction

To detect the antibacterial activity of the prepared samples, solution and film. States were used for each ratio. Every sample was undergo to activity to Escherichia coli (E-coli) and Staphylococcus aurous (staph Ella) microorganisms as shown in figure (2). It is clear that pure I2 is very active in inhibition the growth of both E-Coli and Staph Ella Microorganisms, where the inhibition zone diameters are 30 mm and 40 mm respectively for I2 solution (table 5). In contrast, pure PEG and pure Chitosan have no activity in inhibition the growth of both the two organisms (inhibition zones are zero). For 6 wt% I2 film , the inhibition zone increased from 0 to 10 mm with E-Coli microorganism and from 0 to 15 mm with Staph Ella microorganism. By increasing I2 content in both solution and films, the inhabitation zones increased, which indicate that I2 have good ability to inhibit the growth of these microorganisms. This is clear , where the diameter increased up to 16mm in 10 wt % I2 solution with E-Coli microorganism. Similar behavior occurs with staphella microorganism, where the diameter increased up to 20 mm for the 10 wt. % I2 (solution and film states).Same behaviors occur in film states where the diameter increased up to 20 mm for the 10 wt. % I2 mixture with both the two microorganisms.

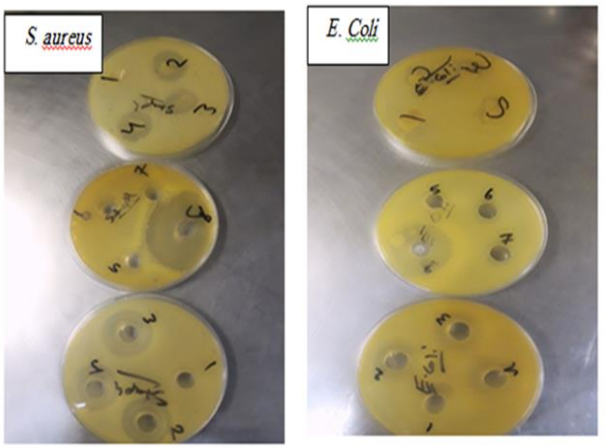


Figure 2. Antibacterial for activities pure I2 , pure PEG , pure chitosan and (PEG / Chitosan / I2) mixture (films and solutions) against E-Coli and S. aureus microorganisms

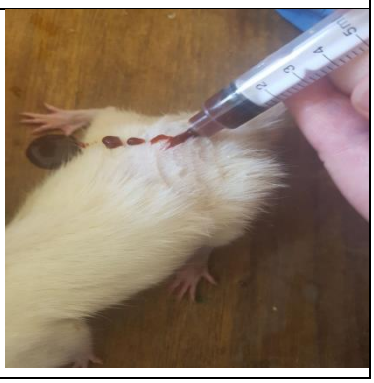
Figure (3) shows the effect of PEG / Chitosan / 10 wt. % I2 film on the health of injured rats, where rats were divided in three groups (each group with three rats) . The first group (a) considered as negative control (without treatment) , the second group (b) as a positive control with celavix drug, while in the third group (c) the PEG / Chitosan / I2 mixtures where added to the injured rats. The addition of the above mixtures done to rats by 6, 8, 10 wt. % I2(figure 3 shows only the 10 wt) . % I2 ratio because it is the best

March-April 2020
ISSN: 0193-4120 Page No. 11107 - 11115

ratio in healing the wounded rat) . The healing tendency for all samples was monitored daily by taking photos. On the second day, there was an improvement in the healing of wounds especially those treated with PEG / Chitosan / 10 wt. % I2 mixture sample as shown image (c),while the animals without treatment (negative control) showed no healing improvement; the wound still wet, redness and there is some coagulation as shown in image (a). After the fifth day of treatment, the images showed that the wound treated with PEG / Chitosan / I2 mixtures looked smaller and the wound healing was better and the skin returned to its normal color, light pink to in picture (c), while the wounds appeared in the animals of group (b) are still in the coagulation stage despite the using of a disinfectant wet as well as with the animals in the untreated group (figure 3 a) .In the seventh day, complete healing of the wound is appeared as shown in photo (c) and the skin return to its nature, while other groups still in coagulation phase as shown in photos (a) and (b).

Table (5) Inhibition zone for diametersfor pure I2 , pure PEG ,pure chitosan and their mixtures

Sample	Inhibition zone diameter (mm)		Sample state
	E-Coli	*S. aureus*	
I_2	30	40	Solution
Pure PEG	0	0	Solution
Pure chitosan	0	0	Solution
6 wt. % I_2	10	15	Solution
	14	18	Film
8 wt. % I_2	15	16	Solution
	16	19	Film
10 wt. % I_2	16	20	Solution
	20	20	Film

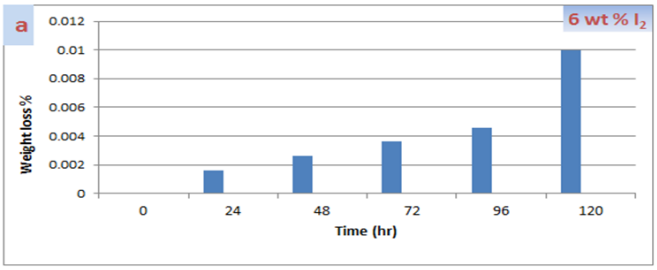
Days	(a)	(b)	(c)
1st			

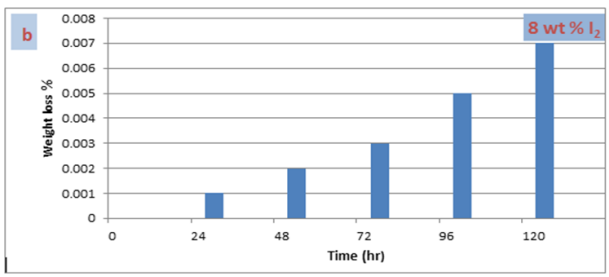
March-April 2020
ISSN: 0193-4120 Page No. 11107 - 11115

Figure 3.Mointering of the health state on the injured rats (a) control negative (b) control positive (c) injured treated by PEG / Chitosan / 10 wt % I2

3.2 Weight loss result

Figure (4) shows the weight loss due to subjecting the prepared films tosun light for 120 hr. It is clear that all samples lose their initial weights dueto sublimating of I2. The samplewith the 6 wt. % I2 losses 91 % from its initial weights, while the 8 wt. % I2 sample losses 93 % and the 10 wt .% I2 sample losses 95 % .This behavior proved the I2 sublimation assumption, which means that I2 with time leaves the polymeric film towards the injured tissue and enhance the healing action.





March-April 2020
ISSN: 0193-4120 Page No. 11107 - 11115

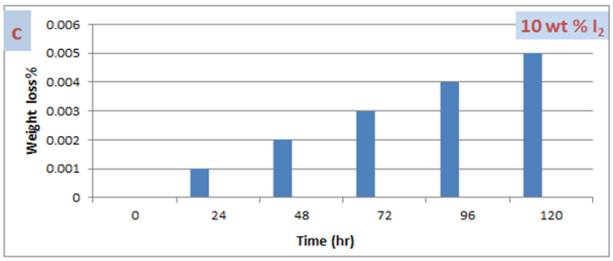


Figure 4. Weight loss for (a) 6 wt. % I2 (b) 8 wt. % I2 (c) 10 wt. % I2

3.3 Optical microscope results

Figure (5) shows pictures with two magnification powers of pure (PEG / Chitosan blend and its composites (6 , 8 and 10 wt % I2). Results showed that the addition of Iodine to the (PEG /Chitosan) blend result in coloration of the film and the color of this film becomes more degree, as well as the magnification increase the distribution of Iodine becomes more clear.

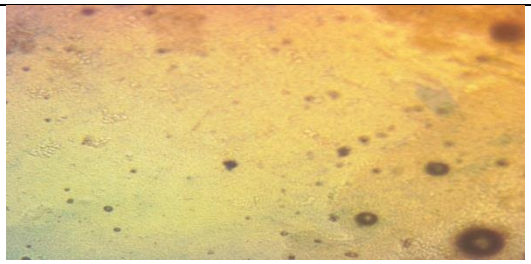
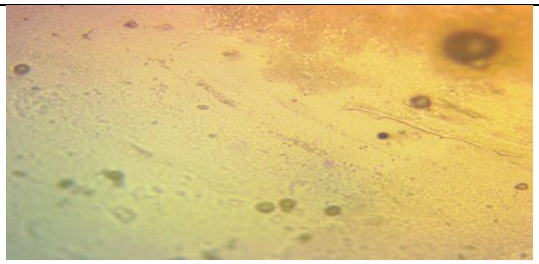
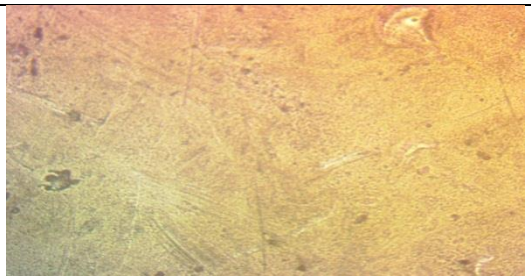
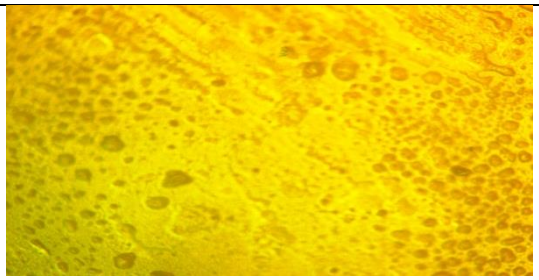
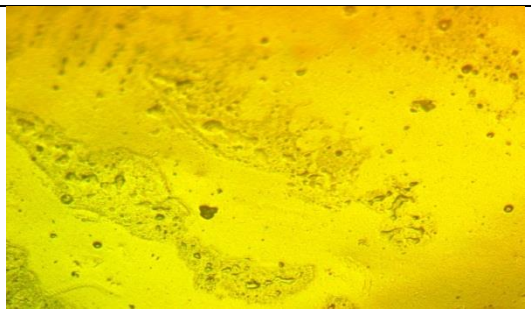
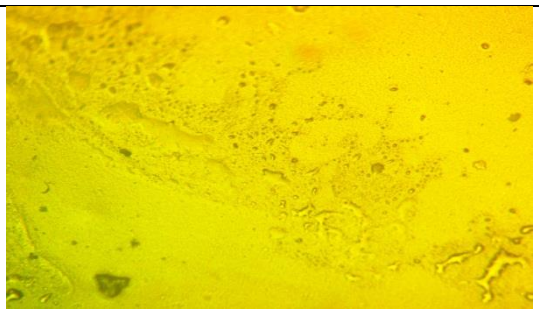
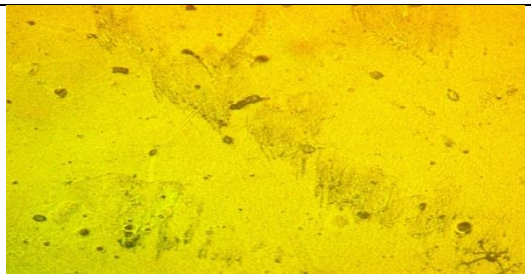
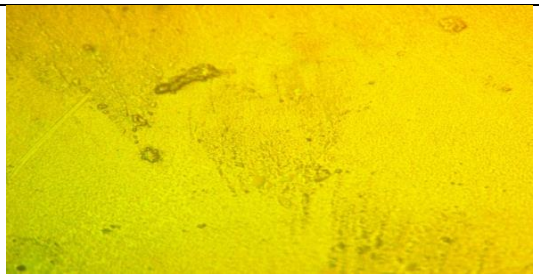
	A	B
PEG /Chitosan blend		
6 wt. % I_2		
8 wt. % I_2		
10 wt. % I_2		

Figure 5. Picture of pure PEG /Chitosan blend and its composites for a-10x, b-20x magnification power

March-April 2020
ISSN: 0193-4120 Page No. 11107 - 11115

3.4 Density results

Figure (6) shows the density behavior of the PEG / Chitosan / I2 mixtures , which increased as the iodine percent increased. This is due to the high Iodine density (5 g/cm3) as well as to the I2 diffusion between PEG / Chitosan chains to fill the vacancy present in this blendnetwork , which resulted in increasing the composite densities .

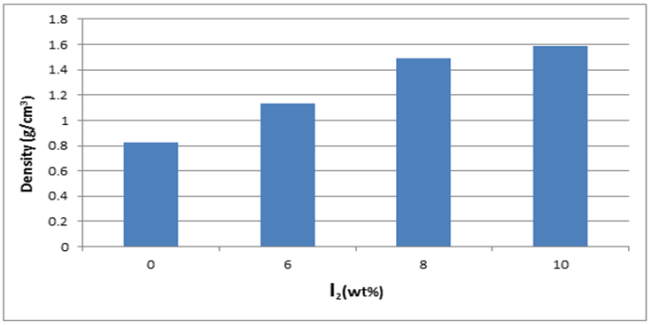


Figure 6. The dependency of density on the I2 content for the prepared samples

3.5 Micro-hardness results

Figure (7) shows that the micro Vickers hardness of PEG / Chitosan and (6, 8, 10 wt. %) I2 composites. It increases with increasing content of I2 under applied load (0.49 N) due to the I2 particles fill the holes and orient the chain therefore hardness increasing .

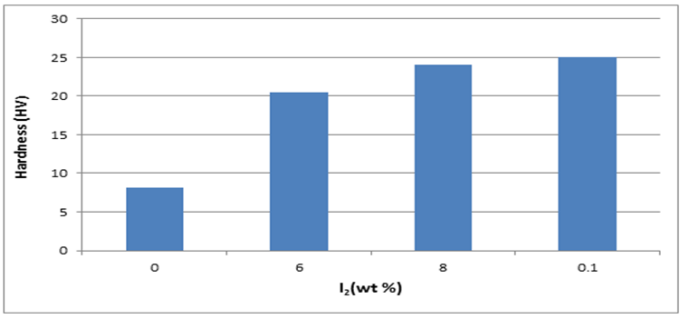


Figure 7. Micro Vickers hardness of neat chitosan - PEG blend and it's composites

3.6 Wettability results

Figure (8) shows the contact angles of PEG/Chitosan blend with it is composites. It is clear the composite wettability behavior with time. In short time; (60 s), the behavior of the film is hydrophobic and slowly its absorptivity increased through the diffusion of water molecule in the filmand the Iodine molecule enhance the diffusion process. Figure 8shows also, that the wettability increased as weight percent of iodine increased.wettability of composites increases with addition of Iodine due to thediffusion in the network of PEG / Chitosan and absorbs water.

Time / sample	At 50 s	At 160 s
a	80.720º	79.80º

March-April 2020
ISSN: 0193-4120 Page No. 11107 - 11115

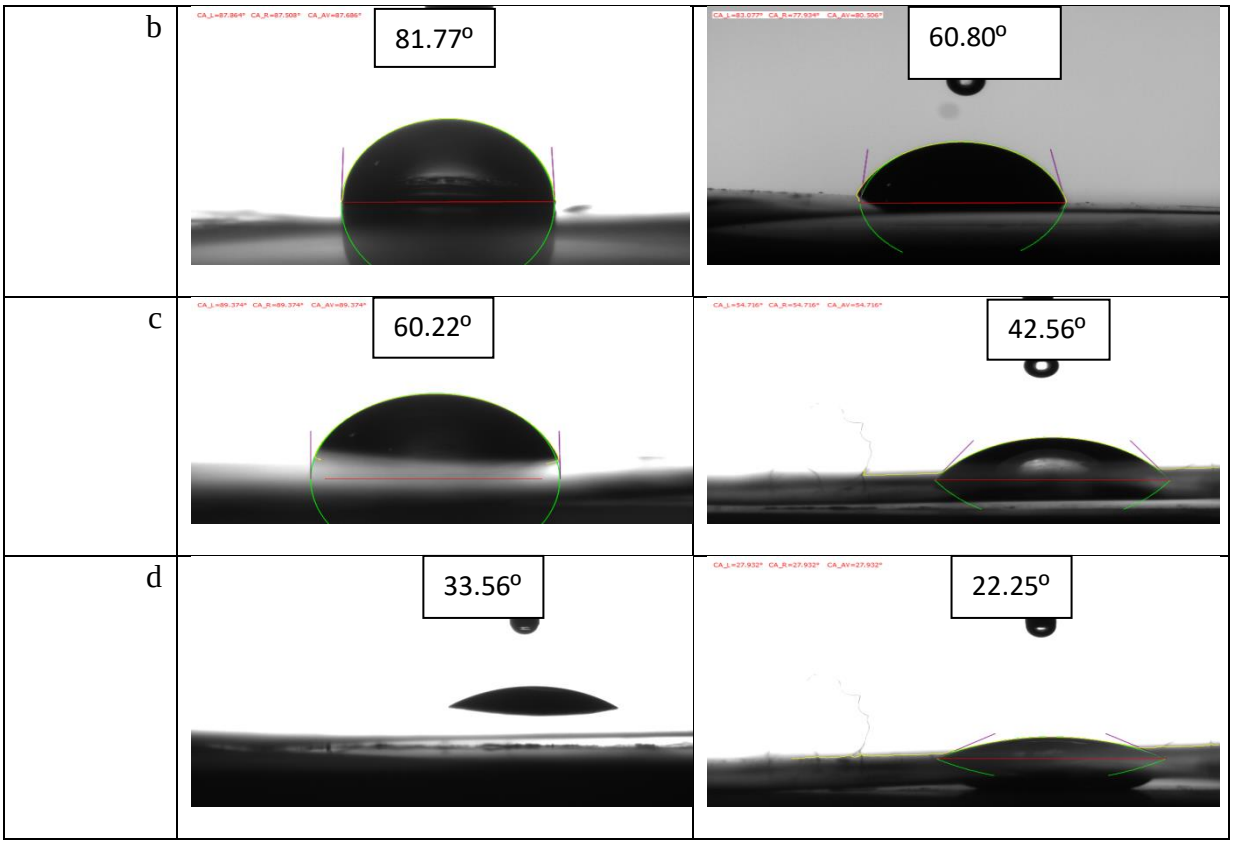


Figure 8. Contact angles at 50s and at 160s for (a) pure blend (b) blend with 6 wt. % I2 (c) blend with 8 wt. % I2 (d) blend with 10 wt. % I2

IV. CONCLUSIONS

From this work, it can be summarize the following conclusions:

1-Iodine has the ability to inhibit the growth of both Escherichia coliand Staphylococcus aureusmicroorganisms.The antibacterial activity of Iodine increasing as Iodine percent increases . The healing action for injured rat's with the prepared films is better than for celavixtreatment ,and the complete healing achieved within seven days for the film state .

2- The weight loss of the film due to sublimation of Iodine is a function of time and stopped after 120 hrs.

3- Density, wettability and color of the composite film increased as I2 percent increased.

4-The wettability of the film increases as time and I2 content increased .

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