Preparation of some gels polymeric networks sustained drug Prednisolone anti-inflammatory and study as Slow release (in vivo) and (in vitro)

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Abstract

six were prepared polymer gel networks retina and retinal semi interference different proportions, namely:

1 - (Starch-g-(PAA-CO-MBA)$_n$ P1
2- (Chitosan + Gluteraldehyd) P2
3- (Chitosan + sebacoylchloride) P3
4 -(Chitosan +70% PEG + Gluteraldehyde) P4-4
5- (Chitosan +70%PEG+ Sebacoyl chloride) P5-4
6 - (Starch-g-(PAA-CO-MBA)$_n$+70% PEG) P6-4

The results showed that polymeric network effect (P5-4) loaded with a drug Prednisolone prevented constitute the updated material carrageenan and xylene, far behind the moral of the tumor ($P < 0.05$) at the time of 0.5, 1 hour, far behind the highly significant ($P < 0.01$) at the time of 2.4, 6, 8.10 The event lasted up to 23 hours from the start of the dosing time. When studying the effect of an anti-inflammatory chitosan it observed the emergence of significant differences ($P < 0.05$) after 0.5, 1, 2.4 & 6 an hour and a highly significant ($P < 0.01$) after the time of 8.10 & 23 hours from the time of dosing. As the drug Prednisolone unit led to obtain significant differences ($P < 0.05$) after 0.5 & 1 hour and a highly significant ($P < 0.01$) after 2 & 4 only an hour of the dosage time, then it observed decline in its influence as an anti-inflammatory, which runs to the end of the experimental period.

Introduction

To date, oral delivery is still the preferred route of drug administration, especially for chronic patients where repeated administration is required. Oral administration offers less pain, greater convenience for patients, higher compliance, and reduced risk of cross-infection and needle stick injuries [1, 2]. Controlled drug delivery technology using natural biodegradable polymers as carrier represents one of the most rapidly advancing areas of science. Poly(esters), polyacrylate, natural gums, and polysaccharides are used for controlled release drug delivery device because these are biodegradable, nontoxic, freely available, and less expensive polymeric materials for use in controlled drug delivery system [3–5]. However, these materials have certain drawbacks, like uncontrolled rate of hydration, unusual thickening, drop in viscosity on storage, and microbial contamination and they require functionalization/modification to overcome these problems. The use of natural gums such as xanthan gum [6], guar gum [7], gum Arabic [8], and gellan gum [9, 10] and polysaccharides such as chitosan, pectin, chondroitin sulphate, cyclodextrins, and dextrose in drug delivery devices is well documented.

Prednisolone,(11ß)-11, 17, 21-trihydroxypregna-1, 4diene-3, 20-dione is a steroidal drug with predominant glucocorticoid and low mineral corticoid activity, as shown in figure 1.

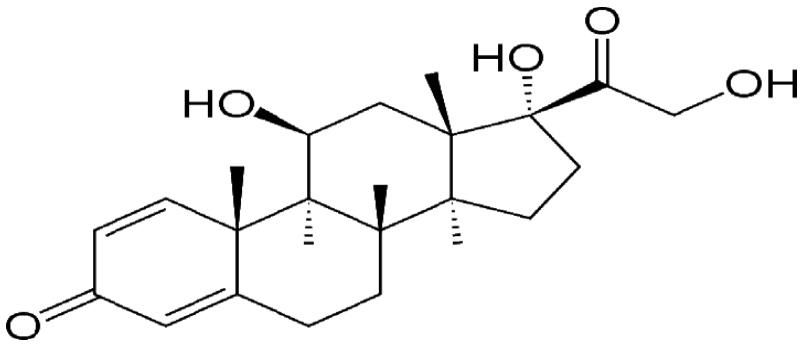


Figure 1. Prednisolone (11ß)-11, 17, 21-trihydroxypregna-1, 4diene-3, 20-dione

It is mainly used for the treatment of a wide range of inflammatory and auto-immune diseases [11-12] such as asthma, multiple sclerosis, rheumatoid arthritis, autoimmune hepatitis etc… [13]. Prednisolone a very slightly water soluble glucocorticoid. So the potential of liquisolid systems to improve the dissolution properties of water-insoluble agents was investigated using prednisolone as the model drug in some study.[14] Prednisolone is also known as ‘disease modifying anti-arthritic drugs’ because of its anti-inflammatory [15] action by inhibiting gene transcription for COX-2, cytokines, cell adhesion molecules, and inducible NO synthase [16].

MATERIALS AND METHODS

Chemicals

All chemicals were purchased from Sigma-Aldrich Co. (St. Louis, MO), and solvents were from E. Merck (Darm-stadt, Germany). All of the reagents were prepared in deionized distilled water to eliminate the contamination of metal ions.

Animals

Inbred colony of adult male and female Swiss albino mice (20-35g) of either sex were used for both anti-inflammatory. They were housed in polypropylene cages under a 12 h light**:**12 h dark cycle in a controlled temperature room (25 ± 2 °C). All the animals were acclimatized to the laboratory conditions for a week before use.

Preperation of Starch-g-(PAA-CO-MBA)$_n$

Starch (2.0 g) was added to 3-neck reactor equipped with a mechanical stirrer , including 35 mL of doubly distilled water . in order to homogenize the starch solution and to decompose the thermally [17] dissociating initiator , i.e . APS, the reactor was immersed in a thermostated water bath preset to 80°C. A definite amount of APS solution (0.1 g in 5mL of H_2O) was then added to the starch solution and was allowed to stir for 10 min. After adding the APS , certain amounts of AA (AA:1.50 g) were added simultaneously to the starch solution . MBA solution (0.05 g in 5 mL of H_2O) was added to the reaction micture after the addition of monomers and the mixture was continously stirred. After 60 min the reaction product was allowed to cool to ambient temperature and neutralized to pH 8 by the addition of 1N sodium hydroxide solution. After 50 mg of $NaHCO_3$ was added , the mixture was stirred to yield an evenly bubbling formation and to accelerate the hydrogel formation. The hydrogel Starch-g-(PAA-CO-MBA)$_n$, was poured to excess in non solvent ethanol (200mL) and kept for 3 h to de water. The ethanol was then decanted and the product was cut to small pieces. Again, 100mL of fresh ethanol was added and the hydrogel was kept for 24 h. Finally, the filtered hydrogel was dried in an oven at 60°C for 10h. After

grinding using a mortar, the powdered superabsorbent was stored away from moisture , heat , and light.

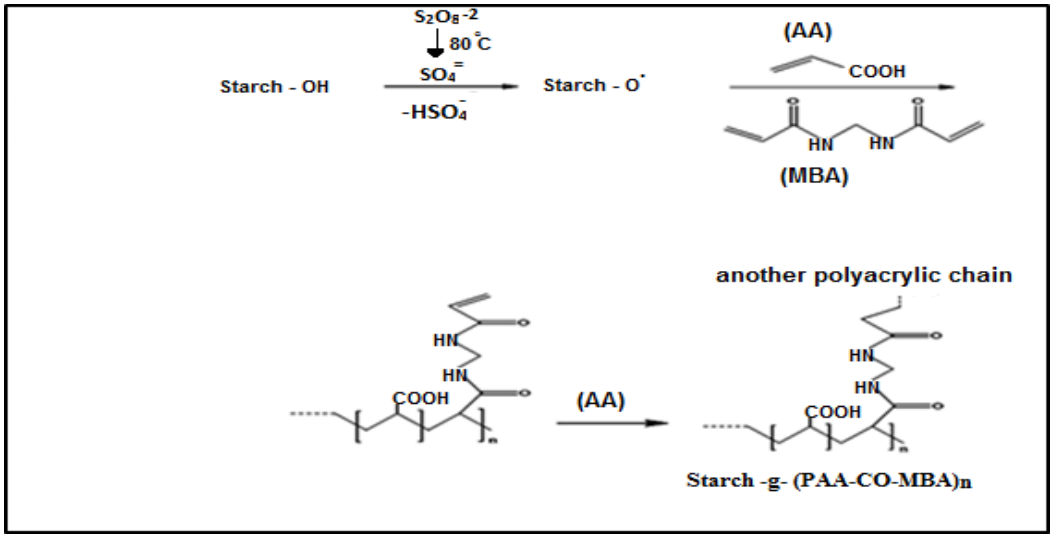


Figure 2. Preperation of Starch-g-(PAA-CO-MBA)$_n$

Preperation of Hydrogel Polymers

The recipes of Chitosan it intertwines chemically through totals Secretary interaction with Alaldhaydat or Chloredat Alasaal, and this is done by adding (80 mg / ml) from the worker clamp (Glutaraldehyde) or (sebacoyl chloride) to a solution consisting of (2% w / v) of Chitosan dissolved in (0.1 Molara) of acetic acid and then add a few drops of (0.1 Molara) of sodium hydroxide to neutralize the solution leaving the mix for two (15 minutes) until they are polymeric network, then nominated mix and wash the precipitate several times in distilled water and then left to dry, then was Bottoming in tablets (8 × 11 mm) under pressure (10 tons) in pressing device, to be used in the swelling test [18]

Preparation of chitosan gels with polyethylene glycol

Was prepared gel networks of Chitosan interlaced with Glutaraldehyde the existence of different ratios with (PEG), Which (10%, 30%, 50%, 70%) as well as the preparation of a gel networks of Chitosan interlaced with Sebacoyl chloride existence of different ratios with Poly ethylene glycol (PEG), Which (10%, 30%, 50%, 70%) as

add these percentages before adding tangles factor, and has solutions equation by adding (0.1 Molara) of (NaOH), then nominated gels formed and washed several times with distilled water then left the air. to dry. I worked with a CD-removal (11 × 8 mm) under pressure (10 tons), the pressing device and then swelling ratio is measured by the models.

Prepare a gel from the gel networks modified of starch (P1) with polyethylene glycol

It was prepared gel networks of gels axis of starch (P1) with Poly ethylene glycol different proportions of (PEG) (10%, 30%, 50%, 70%) by mixing the gel axis with Poly ethylene glycol dissolved in acetic acid and then leaves to dry, then compressed in tablets (11 × 8 mm) under pressure (10 tons) in pressing device, and then use the discs to test the Swelling.

Download drug on gels lecture networks

Was loaded gels (chitosan interlocking with glutaraldehyde and Sebacoyl chloride) and gels network (P4-4) and (P5-4) in addition to the network (P6-4) as well as gels network of modified starch (P1), it has been dipping These polymeric networks in Prednisolone's dissolved in water solution to suck prepared networks required quantity of the property, then leave to dry output, has been pressing the resulting form of tablets (11 ×8 mm) under pressure (10 tons) in pressing for the study of the launch of the drug device.

Anti-inflammtory study
Carrageenan-induced paw edema

Laboratory mice were divided into four groups by six mice (3 males and 3 females). The first group (C) was considered as a control group Dosage orally (10ml / kg) of material (2% Tween 80) The second group (S) and third (T1) and fourth (T2) has Dosage orally (0.16 gm / kg) of the drug Prednisolone, Chitosan, Prednisolone support on polymeric prepared respectively the network. After half an hour of the time the dosage was injected (0.1ml) of material Carrageenan (1%) under the subcutaneous skin in the flat area lining to the left paw. was measured size of the paw using Plethysmometer (Ugo Basile , Italy, Model 7140) after (0.5, 10.8, 6.4, 2 ,1 to 23 hours) of the dosage has been effective anti-inflammatory measure the percentage

rate to discourage developments in size of the paw the increase by applying the following equation:

% inhibition = [1 – Vt /Vc] × 100

Where Vt and Vc represent the increase in paw volumes of mice treated with drug and control, respectively[19].

Xylene-induced ear edema

This study used four groups by six mice (3 males and 3 females). The first group (C) I came back as a group control Dosage orally (10ml / kg) of material (2% Tween 80) The second group (S (and third (T1) and fourth (T2) has Dosage orally (0.16 gm / kg) of the drug Prednisolone, Chitosan, Prednisolone support on polymeric prepared respectively the network . After half an hour of giving dosage , it was placed 0.03 ml of Xylene material on the exterior and interior right ear of the mice, and the left ear was left for comparison . Mice were killed by cutting spinal cord after only four hours later, both were removed from the body of the mouse ears. I took a circular clips by using Cork Borer 7mm in diameter was accurately calculate weights using a sensitive balance to see an increase in gross weight when using xylene Inflamer (Irritant). Returned experiment on other groups of mice were the period of time that mice are then killed (23 hours) from the dosage seemed measured the effectiveness of anti-inflammatory applying the following equation [20]

% inhibition = [1 – Vt /Vc] × 100

Where Vt and Vc represent the increase in paw volumes of mice treated with drug and control, respectively.

Statistical analysis

The data was expressed as mean values ± SEM. and all the data tested with analysis of variance followed by Dunnett's t-test. P-values < 0.05, 0.01 were considered to be statistically significant.

Rusults and Discussion:

Swelling Ratio Study for Prepared crosslinking polymers

Results show described in Figure (3) to (8) that the highest percentage was in the Simulated swollen stomach liquid solution (SGF), and distilled water (H2O) and finally the default intestinal fluid solution (SIF). As it was the highest percentage of the swollen in the polymeric network (P5-4) and a lower proportion of swelling in the polymeric network (P2). This means that the polymer swells in the middle acid significantly meaning that this center helps deprotnized amino groups and hydroxylated and thus increasing charges and water molecules are attracted to her, leading to increased swelling ratio[21].

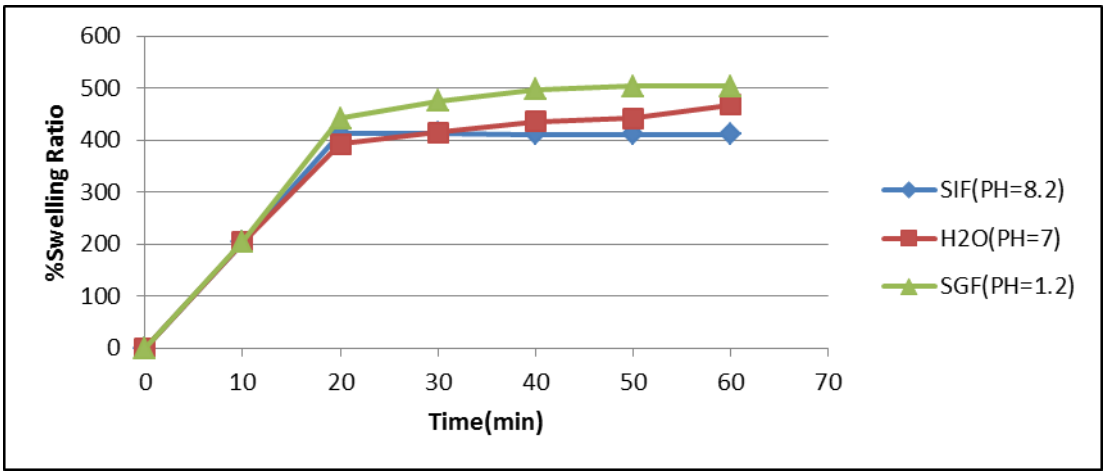


Figure 3. The relationship between the percentage of the swelling hydrogel modified(P1) in the medium of different acidic as a function of time

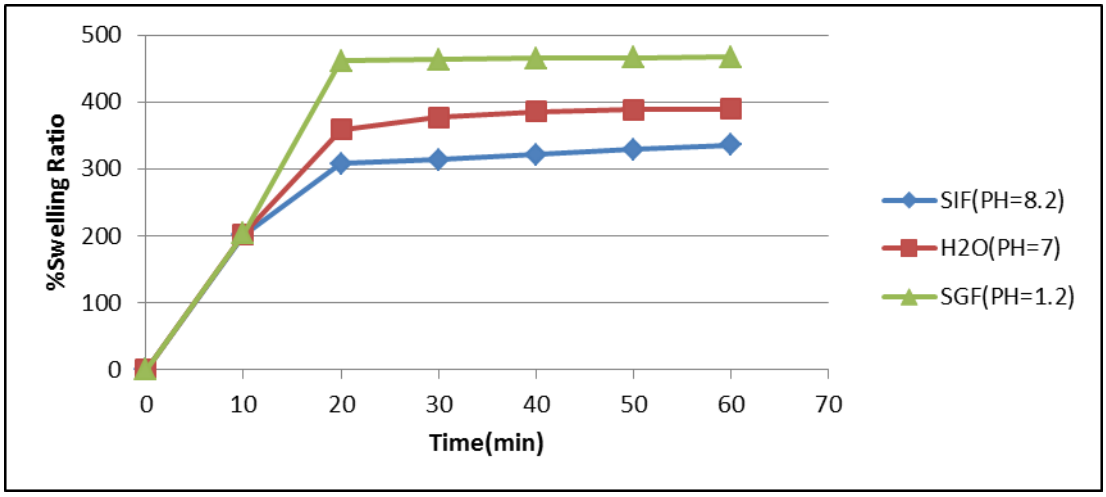


Figure 4. The relationship between the proportion of semi-swollen polymer network interference (P2) among the different acidic as a function of time

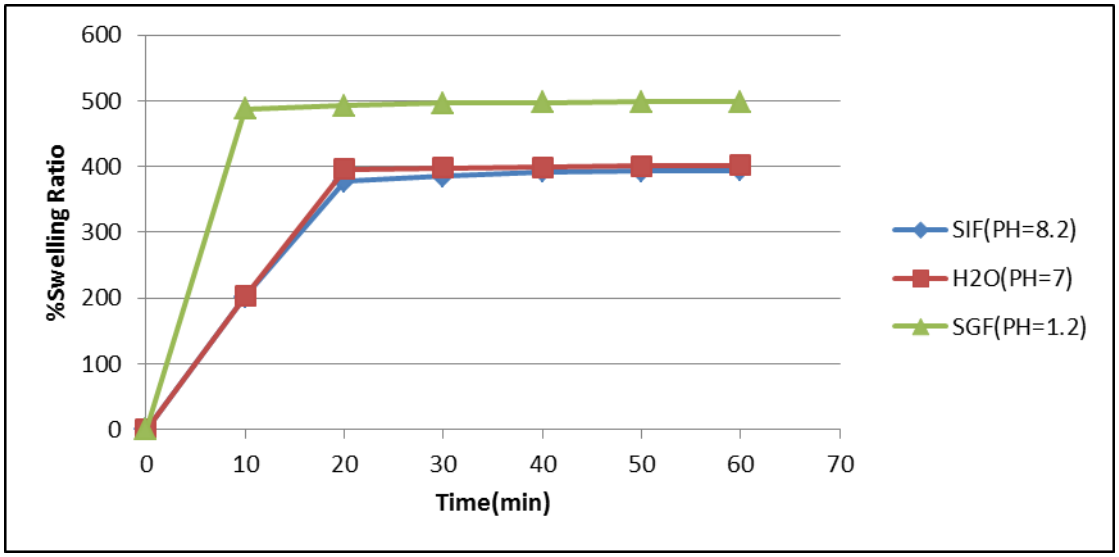


Figure 5. The relationship between the proportion of semi-swollen polymer network interference (P3) among the different acidic as a function of time

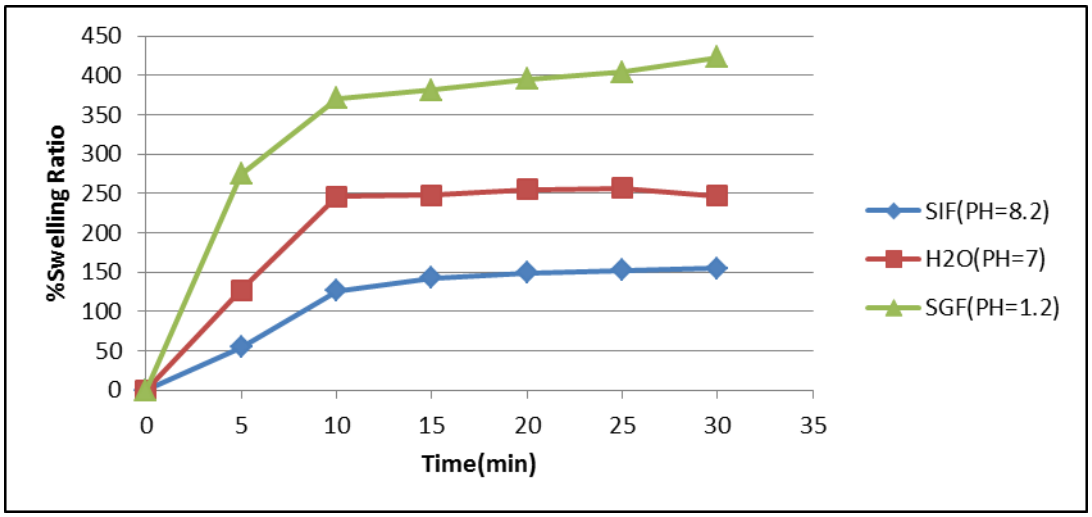


Figure 6. The relationship between the percentage of the swelling polymer network interference (P4-4) among the different acidic as a function of time note that the figure (4) means the polymeric network proportion (70%)

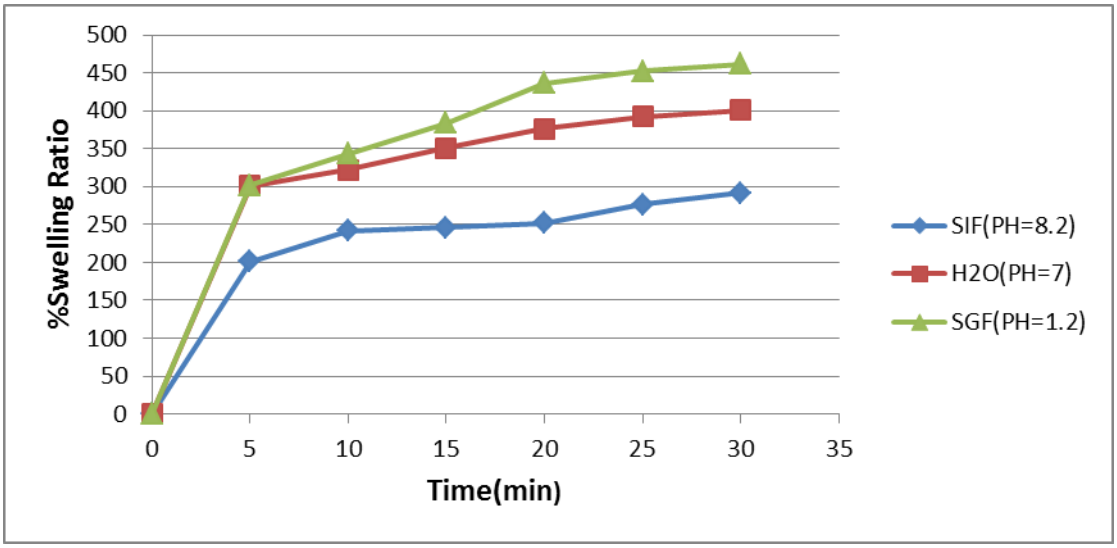


Figure 7. The relationship between the percentage of the swelling polymer network interference (P5-4) in the medium of different acidic as a function of time note that the figure (4) means the polymeric network proportion (70%)

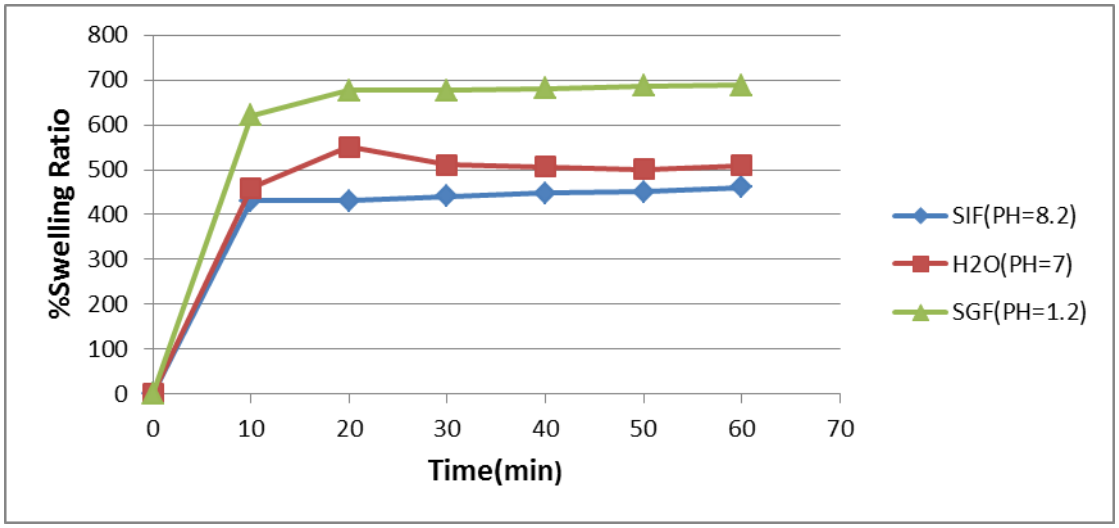


Figure 8. The relationship between the percentage of the swelling polymer network interference (P6-4) in the medium of different acidic as a function of time note that the figure (4) means the polymeric network proportion (70%)

Study the slow release of the drug (Prednisolone) from the prepared systems within the network polymer gels outside(*invivo*)

Results are described in forms (9) to (14) the higher liberation of the drug proportion of the polymers were in Simulated stomach liquid solution (SGF), followed by distilled water (H2O) and finally means the default intestinal (SIF). This is a result of the large bulge Network polymeric in the middle acid, which helps to enter of water within the network and put the drug out in comparison with the center basement, and this is due to the formation of positive ions in acidic solutions that increase the

bonding with water through the formation of bonds of hydrogen and in return will increase water uptake (Water uptake) by the gel lattice [21].

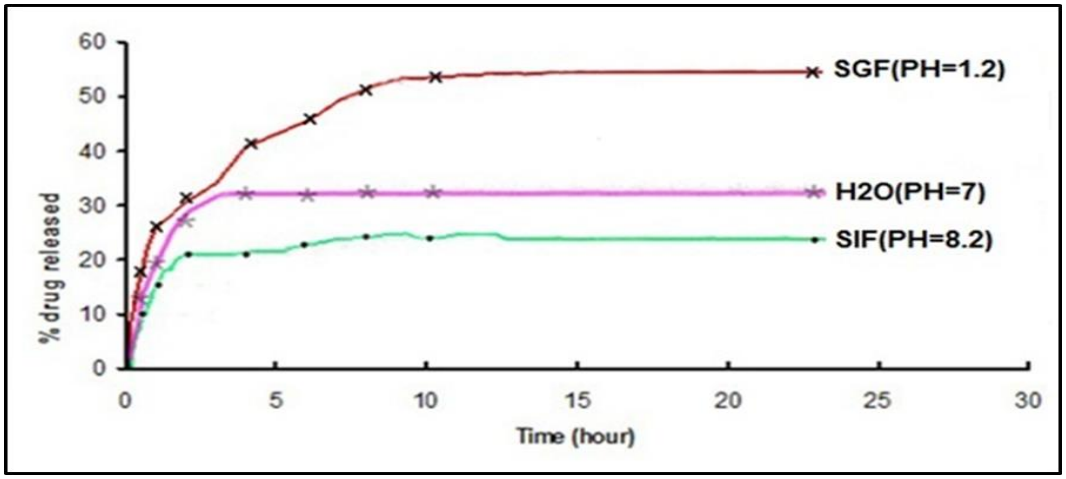


Figure 9. The relationship between the ratio of the drug edit hydrogel modified network (P1) in the medium of different acidic as a function of time

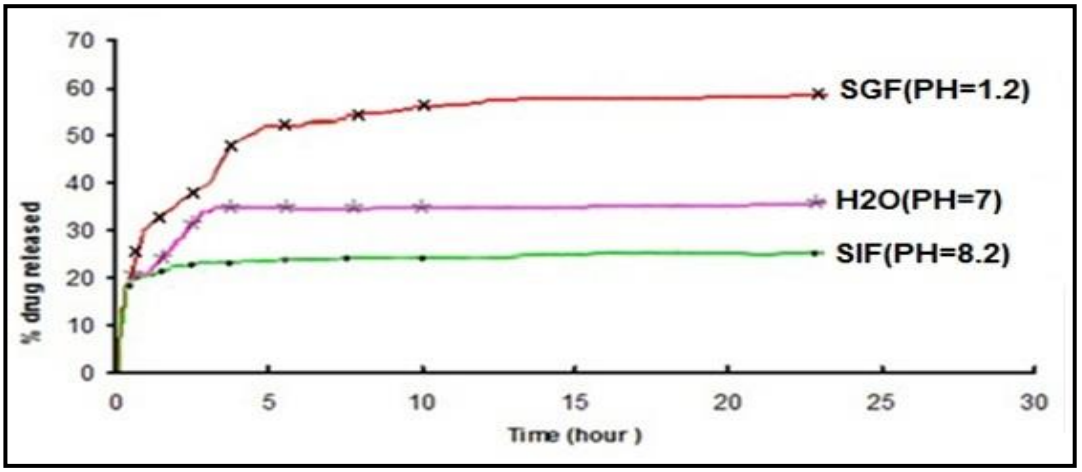
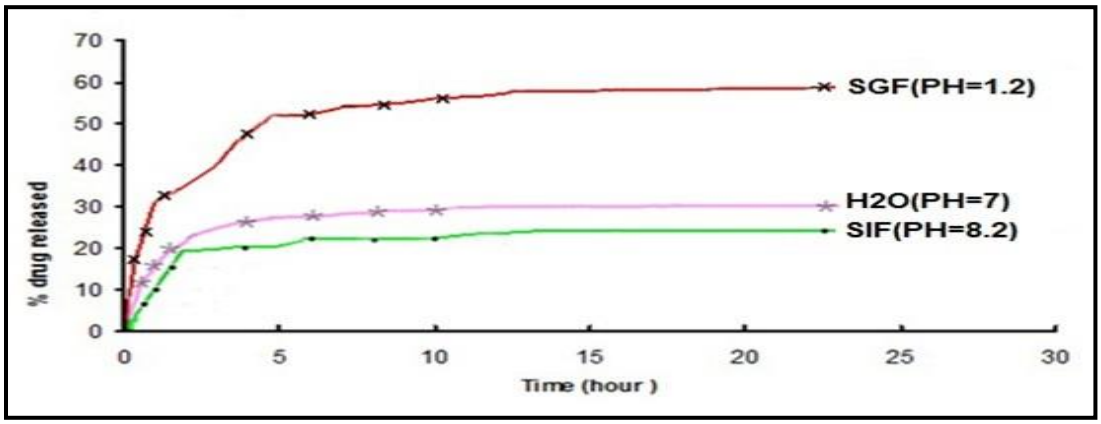


Figure 10. The relationship between the ratio of polymer to release the drug networking intensity interference (P٢) among the different acidic as a function of time

Figure 11. The relationship between the ratio of polymer to release the drug networking intensity interference (P3) among the different acidic as a function



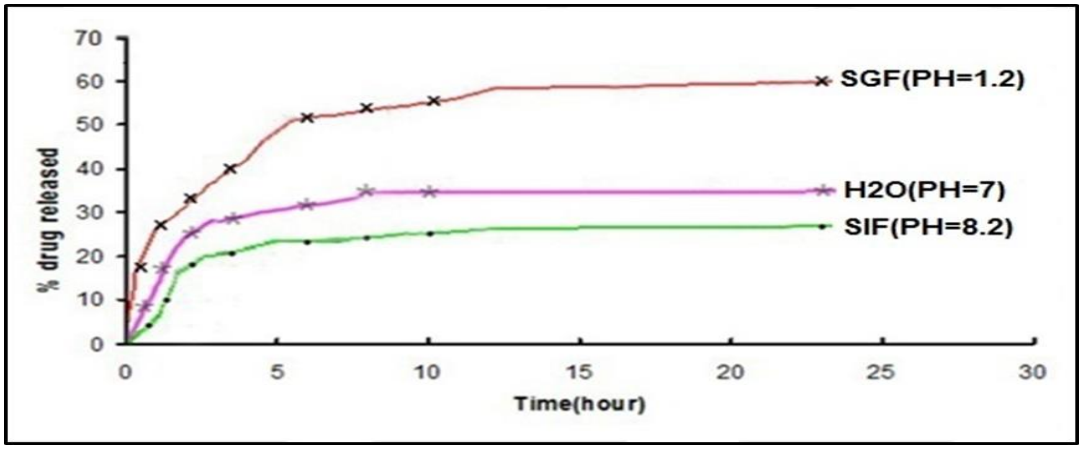


Figure 12. The relationship between the liberalization of the drug polymer network interference ratio (P4-4) among the different acidic as a function of time note that the figure (4) means the polymeric network proportion (70%)

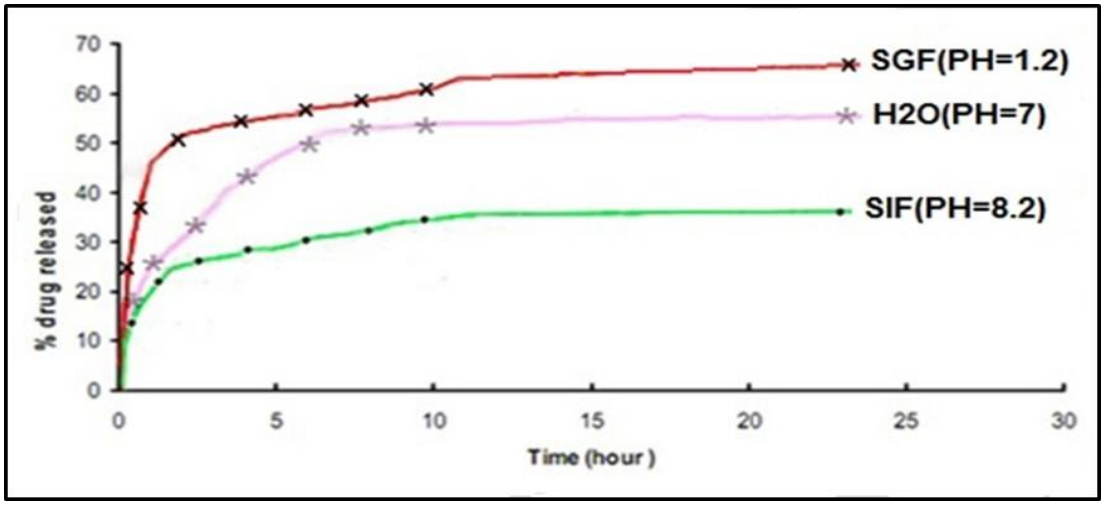


Figure 13. The relationship between the liberalization of the drug polymer network interference ratio (P5-4) in the medium of different acidic as a function of time note that the figure (4) means the polymeric network proportion (70%)

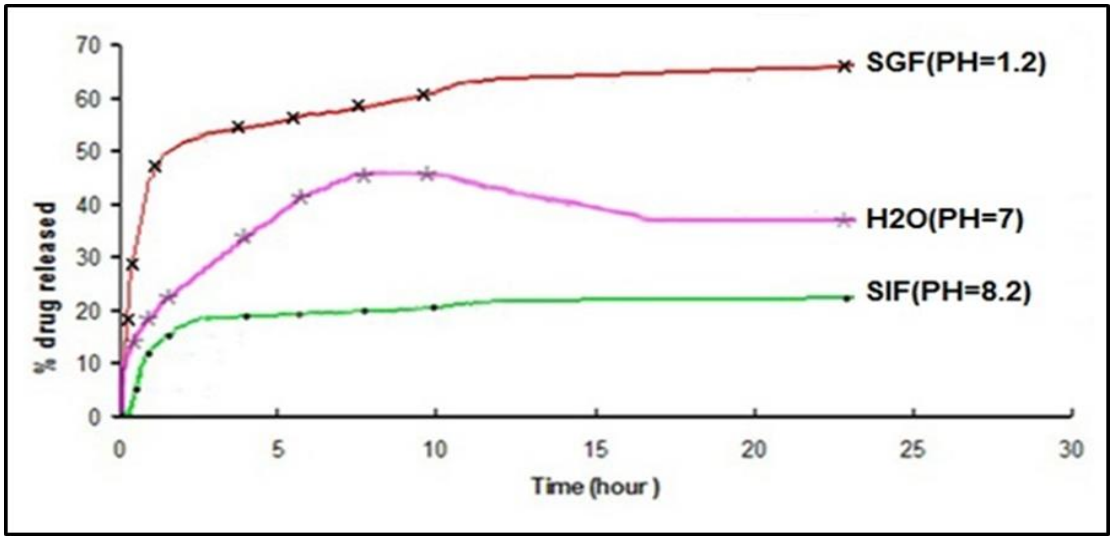


Figure 14. The relationship between the liberalization of the drug polymer network interference ratio (P6-4) in the medium of different acidic as a function of time note that the figure (4) means the polymeric network proportion (70%)

Anti-inflammatory study:

Results showed set forth in the table (1)and (2), respectively, that the polymeric network effect (P5-4) loaded with a drug Prednisolone prevented constitute the updated material carrageenan and xylene and moral difference of the tumor ($P < 0.05$) at the time of 0.5, 1 hour and a highly significant difference ($P < 0.01$) at the time of 2.4, 6, 8, 10 & 23 hours of the start of the dosing time. When studying the effect of chitosan showed significant differences ($P < 0.05$) after 0.5, 1, 2.4 & 6 an hour and a highly significant ($P < 0.01$) after the time of 8.10 & 23 hours from the time of dosing. As the drug Prednisolone unit led to obtain significant differences ($P < 0.05$) after 0.5

& 1 hour and a highly significant (P <0.01) after 2 & 4 only an hour of the dosage time, then it observed decline in its influence as an anti-inflammatory, which runs to the end of the experimental period. Inflammation is a natural response designed to protect the damaged tissue and includes the organization of a complex range of biological processes such as the release of mediators (compounds that mediate inflammation), fluid osmosis, cell migration, and finally crash and repair damaged

tissue cells from inflammation. According to current results, the drug loaded polymeric network (P5-4) showed strong efficacy anti-inflammatory resulting from the updated tumor formation Carrageenan and xylene in laboratory animals [22]. Most of the scientific literature states that the first user test is widely often to investigate new anti-inflammatory is to determine the viability of the compound to reduce the localized tumor updated in the palm of animals by injection of irritating substances [23] The method using xylene in the events of the tumor in the ear of laboratory animals is an important way apply broadly to assess the detachment of vehicles, the size of the affected cells and proliferating vehicles during chronic inflammation. The updated Carrageenan inflammation is an important model to determine the effectiveness of anti-inflammatory compounds used orally.

Table1:polymeric network effect (P5-4) loaded drug Prednisolone when using carrageenan as a catalyst for Edema to stop mice experiment

Represent average values ± standard deviation * P <0.05 ** P <0.01 the number of mice in each group (n) = 6

Table 2: polymeric network effect (P5-4) loaded drug Prednisolone when using xylene as a catalyst for swelling permission to experiment mice

Group symbol	Dosage mg/kg	Ear swelling after 4 hours	Ear swelling after 23 hours
C	Control	6.3	6.4
S	Standard	3.1 ± 0.012** (50.79)	5.6 ± 0.0231 (12.5)
T_1	0.16	4.8±0.311* (23.80)	4.1 ± 0.0131* (35.93)
T_2	0.16	3.4 ± 0.221* (46.03)	2.1 ± 0.0112** (67.18)

Represent average values ± standard deviation * P <0.05 ** P <0.01 the number of mice in each group (n) = 6

Conclusion

Proportion of the drug release of gels lecture networks was good with the dissolution of any balanced medium-term because of owning networks gels prepared good swelling ratios, Acidic function frees significant impact on the drug of polymeric gels rate networks.

Acknowledgments

conversion of most of the chronic diseases drugs to drugs regulated using these systems the fact that the disease of chronic diseases, Connect the drug on other polymers and study within the different communities within the living body (*in vivo*) and outside (*in vitro*) for the development of these systems in terms of efficiency.

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