MediPharm

International Journal of MediPharm Research

ISSN:2395-423X www.medipharmsai.com

Vol.03, No.01, pp 187-194, 2017

"Investigation on swelling parameters of smart biopolymeric hydrogels"

S. Sudarsan[1], D.S. Franklin[2], M. Sakthivel[3], and S. Guhanathan[4]*

[1]Department of Chemistry, Periyar University, Salem-636011,Tamilnadu, India
[1,2]Department of Chemistry, C. Abdul Hakeem College of Engineering and Technology, Melvisharam-632509, Tamilnadu, India,
[3]Research and Development centre, Department of Chemistry, Bharathiyar University, Coimbatore-641046, Tamilnadu, India
[4]PG & Research Department of Chemistry, Muthurangam Government Arts College (Autonomous), Vellore- 632002, Tamilnadu, India

Abstract : Recently, the utilization of renewable resources for the fabrication of bio-based polymeric hydrogels have been explored because of it is eco friendly nature. Polysaccharide based hydrogels has been used enthusing in food industry, pharmaceutical and dental applications due to the availability of natural properties such as gelling agent, thickening agent, soft fragile, non-toxic, biocompatible and biodegradable nature. In this study, Sodium alginate-Triethylene glycol-Acrylic acid hydrogels have been prepared via solventless greener method. Surface morphology and structure of hydrogel evaluated by SEM and FT-IR respectively. Swelling is the most vital parameter for drug delivery, tissue engineering, wound healing and other biomedical applications. Hydrophilic three-dimensional network of bio polymeric hydrogels renders them capable of imbibing large amounts of water molecules due to their ability to swell, when put in contact with a environmentally compatible solvent. Swelling percent, swelling equilibrium, equilibrium water content and swelling in biological fluids can also be investigated in biopolymer by green approach.
Key words: Swelling equilibrium, hydrogels, polysaccharide, hydrophilic, equilibrium water content.

Introduction

Natural polysaccharide was chosen for the preparation of biopolymeric hydrogels due to their low cost and eco friendly, non-toxicity to humans. Ability to form insoluble hydrogels have become more and more significant in various industrial and medical applications, because of plenty of functional groups, they can be simply tailored to yield superior materials[1,2,3]. Hydrogels have the ability to absorb large amounts of water with maintaining their dimensional stability[4,5]. A class of hydrogels which alter its shape, solubility, surface characteristics under the effect of different external conditions such as pH, temperature, ionic strength, solvent composition, light, or electric field, is considered to be a "smart hydrogels" [6,7]. All smart pH sensitive hydrogels are polyelectrolyte contain acidic or basic groups that either accept or release protons in response to changes in pH[8]. Carboxyl groups or amino groups respond to the pH changes by changing their size in the swollen state of biopolymeric hydrogels. At low pH values, the carboxyl containing anionic polymers exhibit minimum ionization and hence reduced hydration of hydrogel. Once the pH of the swelling medium increases in high pH, the carboxyl groups start to ionize and hydrate rapidly, which resulted the expansion and hence it caused higher swelling[9,10].

Sodium alginate (SA) derived from brown algae is an anionic linear polysaccharide composed of poly-β-1, 4-D-mannuronic acid (M units) and a poly-α-1, 4-L-glucuronic acid (G units) in varying proportions by 1–

4 linkages. SA is hydrophilic, biocompatible, and relatively economical due to abundant, renewable, non-toxic, water-soluble and biodegradable[2]. It has been widely used in medical application such as wound dressings, scaffolds materials and environmental related problem such as toxic metal ion and dye removal applications. Tri ethylene glycol (TEG) possessing good flexibility and biocompatibility[11]. Some hydrogels based on poly (ethylene glycol) (PEG) can be considered potential applications due to their excellent biocompatibility and transparency [12,13,14].

Acrylic acid (AA) was used to synthesis a hydrogel with pH-responsive behaviour. Many assessments have shown that AA interactions enhanced the swelling behaviour of hydrogels, particularly in drug delivery systems applications[2,15,16,17,18,19]. AA enhances electrolyte properties due to the carboxyl groups of AA and the ionized carboxylic groups of SA[20].

Our earlier contributions biopolymeric hydrogel synthesised among sodium alginate-ethylene glycol-acrylic acid (SEA) were synthesized[1]. The structure and morphology of the biopolymeric hydrogels were characterized by FTIR and SEM. The swelling properties like swelling percent, swelling equilibrium, equilibrium water content and swelling in biological fluids were also systematically evaluated. In the present investigation triethylene glycol based hydrogels synthesised and characterized thoroughly.

Experimental

Materials and methods

Sodium alginate (SA) (Viscous - average M.Wt: ~ 200,000) was procured from Sigma- Aldrich Company (Bangalore, India). Tri Ethylene glycol (TEG) and Acrylic acid (AA) were purchased from Merck, Pvt. Ltd., India. Demineralised and other chemicals were used without any further purification.

Synthesis of STA biopolymeric hydrogels

Synthesis of hydrogel involved in two steps according to our previous contribution[1,2]. In brief, the synthesis of SA based biopolymeric pH-sensitive hydrogel was done by condensation polymerization followed by free radical polymerization. The polymerization was carried out in a 100 mL three necked flask fitted with a condenser, thermometer, and nitrogen inlet was stirred with a magnetic stirrer. The required amount of sodium alginate and triethylene glycol were dissolved in distilled water. The content was stirred for 1 hr at 80° C in N_2 atmosphere. The completion of the reaction was observed by the formation of pre-polymer. Further, acrylic acid was added to continue the stirring vigorously for next 3 hr in N_2 atmosphere. The formation of yellowish glassy gel implied the completion of the reaction. The resultant hydrogels were submerged in excess distilled water for 2-3 days to remove unreacted monomer and impurities. Then the gel was allowed to dry in oven at room temperature conditioning for 72 hr. The obtained dried hydrogel were collected and stored in air tight container at room temperature till further uses.

Characterization

Sodium alginate and sodium alginate-Triethylene glycol-Acrylic acid (STA) hydrogels were characterized by the following techniques:

Fourier Transform Infrared Spectroscopy (FTIR)

FT-IR spectra of sodium alginate and sodium alginate-Triethylene glycol-Acrylic acid (STA), were recorded in FT-IR spectrophotometer 8400 S.Shimadzu spectrophotometer.

Field Emission Scanning Electron Microscope (FESEM)

To investigate and compare the surface morphology of sodium alginate and sodium alginate-Triethylene glycol-Acrylic acid (STA), SEMs were taken Hitachi SU6600 variable pressure Field Emission Scanning Electron Microscope (FESEM). The samples were mounted on the base plate and gold-sputter coated to render them electrically conductive, the scanning was synchronized with a microscopic beam to preserve the trifling size over a large distance relative to the specimen.

Swelling Studies

The amount of water absorbed by a material is a crucial property, which it has been contributes to biocompatibility and biodegradability. The dried gel swelling experiments were performed in phosphate buffer solutions (PBS) of various pH values ranging from4.0 to 10.0. Swollen gels were removed from the swelling medium at regular time intervals and dried with filter paper, weighed. Known amounts of the dried hydrogel were immersed in solutions of different pH, and the swelling degree and equilibrium swelling were calculated with equation 1 and 2.

$$S = \frac{W_t - W_d}{W_d} \times 100 \qquad (1)$$

$$S_{eq}\% = \frac{W_{eq} - W_d}{W_d} \times 100 \qquad (2)$$

Where, W_d, W_t and W_{eq} are the weights of the sample in the dried state, swollen state

at time 't' and swollen at equilibrium, respectively. The values of S % increased with time, but reached constant value. This value of swelling is called equilibrium swelling (Seq %) [21].

Equilibrium Water Content

The significance of water content in hydrogels at equilibrium is one of their basic properties. A hydrogel with higher water content is generally more advantageous in increasing permeability and bio-compatibility. A lot of work has been dedicated to various aspects such as the swelling and shrinking of non-ionic and ionic gels in aqueous solution, phase transition in gels, the elastic properties of gels and the structure of solvents inside a gel[23]. The water absorbed by the gel is quantitatively represented by the equilibrium water content, EWC (%).

$$EWC\% = \frac{M_{eq} - M_d}{M_{eq}} \times 100 \qquad (3)$$

Where

M_d is the dry weight of the hydrogel and M_{eq} is the hydrated weight of the hydrogel.

Swelling in biological fluids

The swellings of SA based hydrogels in distilled water (DW) and biological fluids such as physiological saline solution(0.89% NaCl), (PS), isoosmotic phosphate buffer in pH 7.4, (PB), artificial (urea) (UR) and the aqueous solution of glucose(1% glucose) (GL) were studied at 37 ^{o}C . Swollen gels, removed from the biological fluids at regular time intervals, were dried superficially with filter paper, weighed. The degree of swelling, S, was calculated as [24] in eqn (2)

Results and Discussion

In this investigation, the SA condensed with TEG to form pre-polymer and then STA yellowish glassy hydrogel produced through the free radical polymerization of AA. These TEG can interact sodium atoms from SA chains to form insoluble pre-polymer. Later, the vinyl groups of AA were prompted onto pre-polymer (SE) pendant backbone to form STA 3D hydrophilic polymeric network. During the polymerization process, AA vinyl groups with initiator $K_2S_2O_8$ can entangle through SA chains to form crosslinked insoluble hydrogels, and the electrostatic interaction and hydrogen-bonding interactions were vital role for the formation of hydrogel.

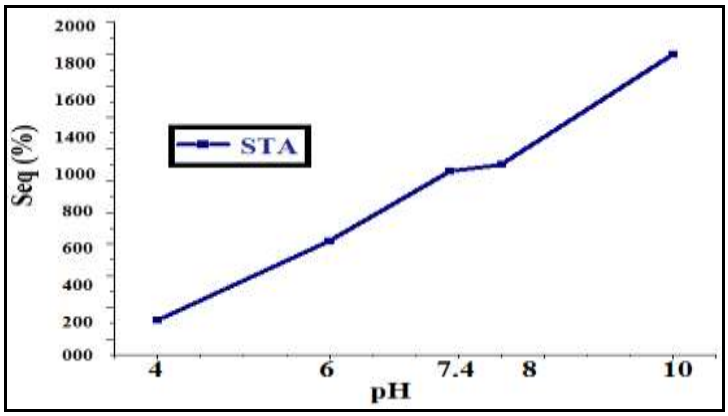

Fig.1. Swelling studies (Seq%) of STA hydrogel at pH 4.0 to 10.0

Swelling Studies

Equilibrium Swelling (S_{eq}%) for various STA biopolymeric hydrogel values was represented in Fig.1. Polyfuncional groups on the SA chains (Eg., carbonyl, carboxyl and hydroxyl) involved the solvent and hydrogel interaction. The (Seq %) values was better with time up to certain level (6 hours), then levels off. This values of swelling might be called equilibrium Swelling (S_{eq}%). Previously, our research group has reported the pH-sensitive hydrogels of Citric acid (CA) and TEG between 4.0 to 10.0. The S_{eq}(%) of tri ethylene glycol (TEG) based hydrogels were pH 4.0=260.00, pH 6.0=368.00, pH 7.4=1000.00, pH 8.0=1020.00, pH 10.0=1450.00 % respectively[3]. The STA biopolymeric hydrogels have demonstrated the pH dependencies of equilibrium swelling at higher pH than lower pH. Swelling behaviour of STA at present investigation were observed in different composition with different pH range from 4.0 to 10.0. The S_{eq} (%) value of STA at pH 4.0=120.00,pH 6.0=620.00,pH 7.4=1060.00, pH 8.0=1102.00, and pH 10.0=1800.00 % respectively. The enhanced swelling was observed due to the polyfunctionality and formation of ester linkage in biopolymeric hydrogel.

Equilibrium Water Content

Fig.2. was showed the one of the fundamental properties of hydrogel contains water in itself at equilibrium. Biocompatibility of hydrogel generally more water content due to the hydrophilic and crosslinked nature of the biopolymer. The water transport was strappingly caused by the presence of ionisation of biopolymeric hydrophilic functional groups, such as –OH, –COOH, –$CONH_2$,–CONH, or –SO_3H, along the hydrogel network[25]. Increasing pH of swelling media resulted in deprotonation of sodium alginate carboxylic groups. Many research work has been devoted to different aspects such as swelling, flexible nature and favourable permiselectivity of water inside a hydrogel [26,27]. The equilibrium fluid content, EWC (%) of STA and its series of hydrogels fluids were calculated by using equation (3). The value obtained in the range of EWC (%) is 65 to 96 %.

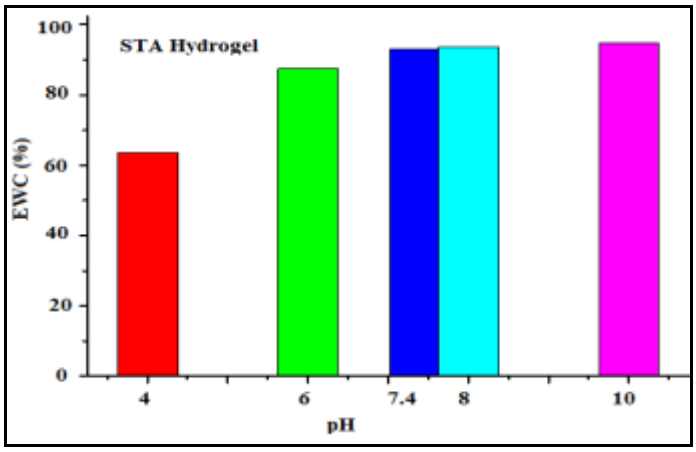

Fig.2. Studies of equilibrium water content (EWC%) in STA hydrogel

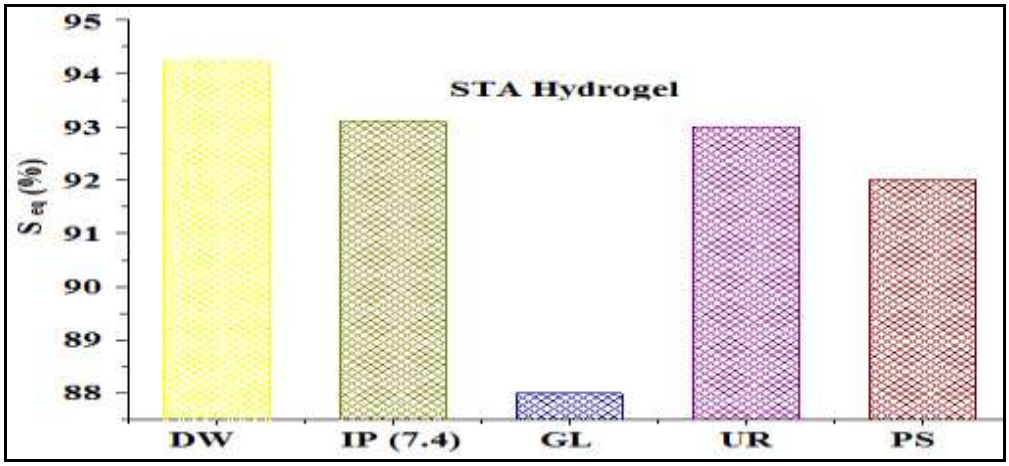

Fig.3. Swelling studies of STA hydrogel in biological fluids

Swelling in biological fluids

The swelling equilibrium has been performed at room temperature in different physiological body fluids such as distilled water (DW), and simulated body fluids such as artificial (urea) (UR), physiological saline (0.89%NaCl solution) (PS), and isoosmotic phosphate buffer in pH 7.4 (IP).The influence of physiological body fluids on its swelling ratio was also observed. Fig.3. was clearly illustrated that the presence of solutes (physiological body fluids) in swelling medium suppress the swelling equilibrium. It is mainly due to the decrease in osmotic pressure of external solution. The S_{eq} (equilibrium swelling) can also be calculated using equation (1). The swelling equilibrium was observed in the following order: DW> IP> UR> PS > GL respectively. This investigation was elucidating the biopolymeric material, when it comes in contact with biological body fluids for the utilization as a scaffold, bone, tissue engineering and drug delivery. Fig.3. are depicted that the swelling ability of hydrogel gradually increased with the increase in time [23].

FT-IR studies

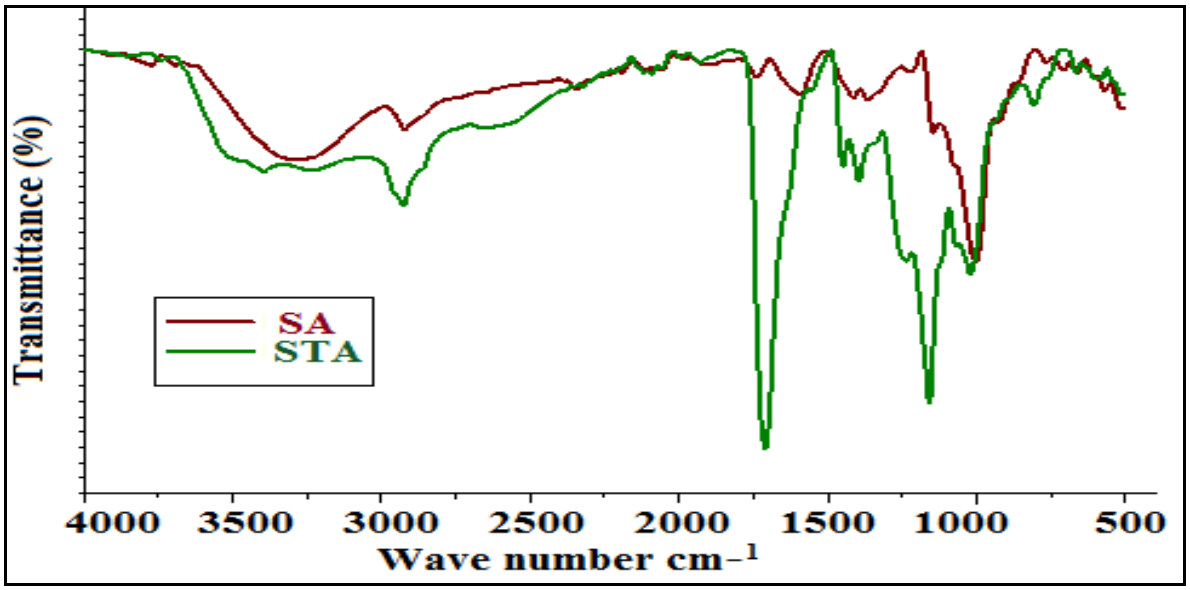

Fig.4. FT-IR spectrum of sodium alginate (SA) and STA hydrogel

The FT-IR spectrum of the pure SA and STA biopolymeric hydrogel were depicted in Fig. 4. The broad stretching peak were observed at 3289 cm^{-1} in SA, corresponds to presence of –O–H stretching vibration of the hydroxyl group in the SA backbone. More broadening of 3409 cm^{-1} stretch obviously states intermolecular hydrogen bond formation within STA biopolymeric hydrogel. The intermolecular hydrogen bonding provides

additional network strength to biopolymeric hydrogel. These differences supported the successful fabrication of triol and acrylic acid onto sodium alginate. Alteration of 1149 cm^{-1} stretching band of SA into a small peak 1030 cm^{-1} absorption stretch in peak of –CH–OH in cyclic alcohol C–O–C stretching present in the FT-IR spectrum of SA are accredited to its polysaccharide ring structure. Asymmetrical stretching vibration at 1602 cm^{-1} in SA showed presence of –COO group. Pure SA exhibits the well-known peaks of C=O of the carboxylic group at 1745 cm^{-1} and the important characteristic peak of free hydroxyl group was observed in the range of 3289 cm^{-1} [28]. The spectrum of STA biopolymeric hydrogel were confirmed by a shift in the C=O peak from1745 cm–1 in the pure SA to 1712 cm^{-1} for the tailored hydrogel. To find out changes in peak intensity or peak shifting that could reveal interaction between atoms. This shift might be due to the ester formation of -C–O- bond and the interaction of hydroxyl group of TEG with COOH group of AA. Such a changes in the spectrum confirmed the successful synthesis of biopolymeric hydrogel [26]

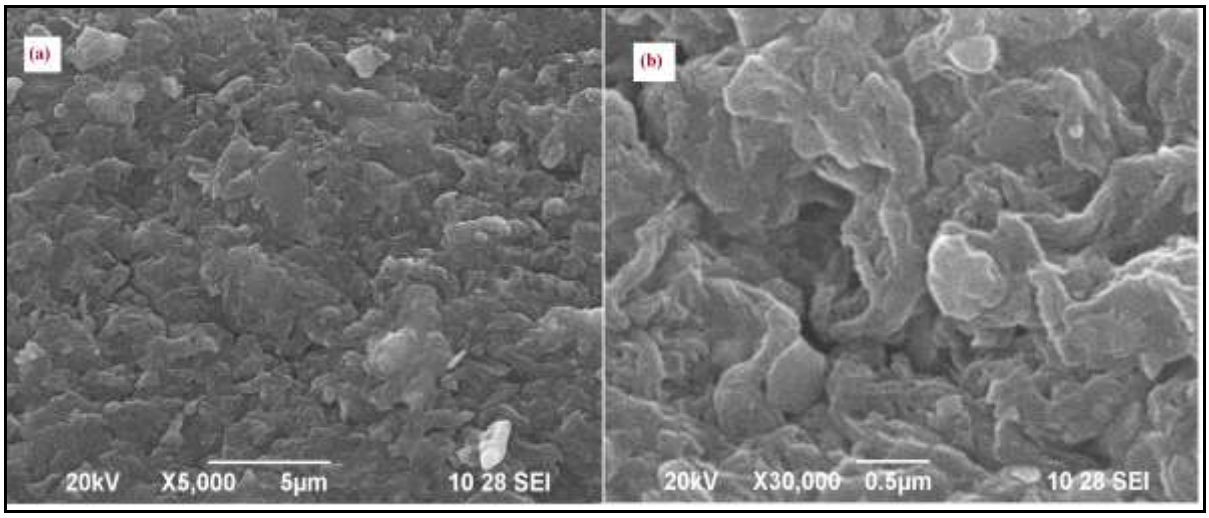

Fig .5. SEM image of STA hydrogels

SEM

Representative SEM images of STA dry hydrogels were presented in Fig.5. The inter connected cavity surface arrangement was present throughout the hydrogels [29]. The uneven rough surface was also observed in STA hydrogel. The morphology of the external surface of STA biopolymeric distorted from smooth surface (Fig. 5a). Also, the SEM images (Fig. 5b) consign the presence of some enlarged aperture of the interior surface of STA hydrogel. Compared with other SA based hydrogels, STA based biopolymeric hydrogels offered a more hydrophilic and precise the microstructure. The cavities and hollowness morphological properties were inclined to offer moderate surface changes, which could be provide a better contact between solution and hydrogels, allowing easier solution uptake and better swelling behaviour.

Conclusion

Polysaccharide biopolymeric STA hydrogel were successfully synthesized by green approach method. The fabrication of cavities hydrogels to enhance the water holding and other solvent absorbing ability. The FT-IR spectrum of STA hydrogel well supported for the formation of hydrophilic network. The results of the Swelling percent, swelling equilibrium, equilibrium water content, swelling in biological fluids measurements and SEM observations consistently confirmed that the polysaccharide hydrogels has been posses' quicker swelling behaviour than the other hydrogels. Swelling has the most vital parameter for drug delivery, tissue engineering, wound healing and other biomedical applications. These kind of the biomaterials recommended that sodium alginate based biopolymeric hydrogels as new materials utilized enthusing in food industry, pharmaceutical, dental and environmental applications.

Acknowledgments

One of the authors, Mr. S. Sudarsan, gratefully acknowledges the authorities of C. Abdul Hakeem College of Engineering and Technology, Melvisharam, Tamil Nadu, India for providing laboratory facilities.

References

1. Sudarsan S, Franklin DS, Sakthivel M, Guhanathan S, Non toxic, antibacterial, biodegradable hydrogels with pH- stimuli sensitivity: Investigation of swelling parameters, Carbohydrate Polymer, 2016, 148: 206-215.
2. Sudarsan S, Franklin DS, Guhanathan S, Imbibed salts and pH-responsive behaviours of sodium alginate based eco-friendly biopolymeric hydrogels- A solventless approach, Macromolecular an International Journal, 2015, 11: 24-29.
3. Franklin DS, Guhanathan S, Simple, convenient, low-cost, and solventless greener way to pH-responsive polymeric hydrogels: Synthesis and characterization, Journal Applied polymer Science, 2014, 1314-1403.
4. Yella S, Vanapu srinivasa rao A, Kalakonda S, Development and evaluation of super porous hydrogel tablets of cefditoren pivoxilas a gastro retentive system, International journal of medipharm research, 2015, 3:166-177.
5. Franklin DS, Guhanathan S, Synthesis and characterization of citric acid-based pH-sensitive biopolymeric hydrogels, Polymer Bulletin, 2014,71: 93–110.
6. Mohy Eldin MS, Omer AM, Wassel MA, Tamer TM, Abd elmonem MS, Ibrahim SA, Novel smart pH sensitive chitosan grafted alginate hydrogel micro capsules for oral protein deivery: I. preparation and characterization, International Journal of pharmaceutical and pharmacy science, 2015,10: 320-326.
7. Mohy Eldin MS, El-Sherif HM, Soliman EA, Elzatahry AA, Omer, AM, Polyacrylamide-grafted carboxymethyl cellulose: smart pH-Sensitive hydrogel for protein concentration, Journal of Applied Polymer Science, 2011,12:469-79.
8. Franklin DS, Guhanathan S, Influence of Chain Length of Diol on the Swelling Behavior of Citric Acid Based pH Sensitive Polymeric Hydrogels: A Green Approach, Journal of Applied Polymer Science, 2014, Doi: 10.1002/App.41403
9. Sudarsan S, Franklin DS, Guhanathan S, Influence of ethylene oxide units on pH and salt responsibility of sodium alginate biopolymeric hydrogels-By Greener approach, International Journal of Frontiers and Science, 2015, 2: 88-99.
10. Kumara A, Srivastava A, Galaev IY, Mattiasson B, Smart polymers: physical forms and bioengineering applications, Progress in Polymer Science, 2007,32:1205–37.
11. Brandl F, Henke M, Rothschenk S, Gschwind R, Breunig M, Blunk T, Tessmar J, Göpferich A, Poly(EthyleneGlycol) Based Hydrogels for Intraocular Applications, Advanced in Engineering Materials, 2007, 9: 12. DOI: 10.1002/adem.200700221
12. Vanaja A, Ramaraju GV, Srinivasa rao K, Role of NaOH concentration on structural, morphological and optical properties of ZnO nanopoder synthesized by sol-gel process, International journal of techno chemical research, 2016, 2:110-120.
13. Franklin DS, Guhanathan S, Performance of silane‐coupling agent‐treated hydroxyapatite/diethylene glycol‐based pH‐sensitive biocomposite hydrogels, Iranian Polymer Journal, 2014, 23:809–817.
14. Dai X, Chen X, Yang L, Foster S, Coury AJ, H Jozefiak TH, Free radical polymerization of poly(ethylene glycol) diacrylate macromers: Impact of macromer hydrophobicity and initiator chemistry on polymerization efficiency, Acta Biomaterials, 2011,2: 1965–1972.
15. Patel S, Patel M, Formulation and evaluation of sustained release pellets of tramadol HCl using different release retarding polymer, International journal of medipharm research., 2015, 2:106-114.
16. Franklin DS, Guhanathan S, Investigation of citric acid-glycerol based pH-sensitive biopolymeric hydrogels for dye removal applications: A green approach, Ecotoxicology and Environment Safety, 2015 121:80-6. DOI: 10.1016/j.ecoenv.2015.05.003.
17. Franklin DS, Guhanathan S, Swelling and salt responsive studies of biocomposite hydrogels via solventless green approach, Research revision polymer, 2015, 6: 005-010.
18. Pourjavadi A, Eftekhar Jahromi P, Seidi F, Salimi H, Synthesis and swelling behavior of acrylatedstarch-g-poly (acrylic acid) and acrylatedstarch-g-poly (acrylamide) hydrogels, Carbohydrate Polymer, 2010, 79: 933–940.

19. Sakthivel M, Franklin DS, Guhanathan S, pH-sensitive Itaconic acid based polymeric hydrogels for dye removal applications, Ecotoxicology and Environment Safety, 2015, DOI :10.1016.2015.11.004*)*.
20. Horia M, El-Din N, Manal F, Taleb A, Wahab A, El-Naggar M, Metal sorption and swelling characters of acrylic acid and sodium alginate based hydrogels synthesized by gamma irradiation, Nuclear Instrumental Methodology Physics Research B, 2008, 266: 2607-2613.
21. Franklin DS, Guhanathan S, Substantial performance of silane surface treated 1,4 butane diol /hydroxyapatite biocomposite hydrogels for dye removal applications, American Journal of Chemical Material Science, 2014, 4: 24-29.
22. Kirubanandan S, Renganathan S, An evaluation of wound repair and regeneration potential of the fruits of phyllanthus emblica (Amla), International journal of medipharm research, 2016, 2:71-81.
23. Shah R, Saha N, Saha P, Influence of temperature, pH and simulated biological solutions on swelling and structural properties of biomineralized ($CaCO_3$) PVP–CMC hydrogel, Bio materials, 2015, 4 :2-4: 123–136.
24. Saraydin D, Çaldiran Y, In vitro dynamic swelling behaviors of polyhydroxamic acid hydrogels in the simulated physiological body fluids, Polymer Bulletin, 2001, 46: 91-98.
25. Tripathi R, Mishra B, "Development and Evaluation of Sodium Alginate–Polyacrylamide Graft–Co-polymer-Based Stomach Targeted Hydrogels of Famotidine", Pharmaceutical Science Technology, 2012, 13: 4, DOI: 10.1208/s12249-012-9824-1.
26. Peppas NA, Franson NM, The swelling interface number as a criterion for prediction of diffusional solute release mechanisms in swellable polymers, Journal of Polymer Science and Polymer Physics,1983, 21: 983–997.
27. Ritger PL, Peppas NA, A simple equation for description of solute release. II Fickian and anomalous release from swellable devices, Journal of Control Release,1987, 5:37–42.
28. Kalyania S, Smithab B, Sridharb S, Krishnaiaha A, pervaporation separation of ethanaol-water mixture through sodium alginate membrane, Desalination, 2008, 229: 68–81.
29. Shi X, Zheng Y, Wang G, Lin Q, Fan J, pH- and Electro-responsive Characteristics of Bacterial Cellulose Nanofiber/ Sodium Alginate Hybrid Hydrogels for the Dual Controlled Drug Delivery, Royal Society Chemical advances, 2012- DOI: 10.1039/b000000x

*****