Application of Alginate in Water Treatment and Drug Delivery Systems

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Declaration

I certify that this thesis does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any university; and that to the best of my knowledge and belief it does not contain any material previously published or written by another person except where due reference is made in the text.

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Wafa Algothmi on _____/_____/_____

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Abstract

This thesis covers both the use of Ca-Alg_2 hydrogels in water treatment and drug delivery system. Ca-Alg_2 and Ca-Alg_2/GO gel bead adsorbents fabricated for the removal of Cu^{2+} ions from aqueous solution. The influence of the use of different adsorbent doses, Cu^{2+} concentrations and contact time on the adsorption process was demonstrated that the larger surface area of GO and oxygen containing functional groups on the GO surface plays a strong role in increasing the adsorption capacity of Ca-Alg_2.

Chapter two discusses the loading of RB, Rubpy and CPT into Ca-Alg_2 hydrogel using the *in situ* addition method. The influence of the pH of the released medium affected on the release of both of dye and drug from Ca-Alg_2 hydrogel. The molecular weight and the charge of the dye or drug play an important role in the releas process from Ca-Alg_2 hydrogel. Furthermore, the release kinetic studies for both of dye and drug revealed that the release mechanisms of the three molecules at pH ~ 2.4 occurred via Fickian diffusion and Case II transport. However, at pH ~ 7.4, the release mechanisms was an anomalous transport.

This thesis also focused on synthesis and characterisation of β-CD-g-Alg. The characterisation of the CPT inclusion complexes (CPT/β-CD and CPT/β-CD-g-Alg) confirmed that the inclusion complexes were produced, and the results indicated that the amino quinoline group for CPT molecule is included into the β-CD cavity. Furthermore, the thermal analysis shows that the ratio of Na-Alg to β-CD appears to

be 2:1. The last section details the release profile of CPT from both inclusion complexes using the dialysis technique, and Fick's second law was used to analyse the release data. It was found that β-CD prolonged the release of CPT with initial burst release and reached the equilibrium after 9 days. However, the release of CPT from the CPT/β-CD-g-Alg inclusion complex did not show the initial burst release and the equilibrium was reached after 13 days. This result indicates that Na-Alg increased the solubility of CPT/β-CD inclusion complex and enhanced the formation of CPT/β-CD.

Publications

Algothmi, W. M., Bandaru, N. M., Yu, Y., Shapter, J. G., & Ellis, A. V. "Alginate–graphene oxide hybrid gel beads: An efficient copper adsorbent material." *Journal of colloid and interface science* 397 (2013): 32-38.

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Lists of abbreviations, symbols and units

Symbol/acronym/unit	Translation/explanation
Na-Alg	Sodium alginate
H-Alg	Alginic acid
G	Guluronic
GDL	D-glucono-δ-lactone
M	Mannuronic
Ca^{2+}	Calcium (II) ions
Sr^{2+}	Strontium (II) ions
Ba^{2+}	Barium (II) ions
pH	Power of Hydrogen (per Hydrogen)
pK_a	Acidic constant
Cu^{2+}	Copper (II) ions
Ni^{2+}	Nickel (II) ions
Co^{2+}	Cobalt (II) ions
$CaCO_3$	Calcium carbonate
Na^{+}	Sodium (I) ions
CNTs	Carbon nanotubes
GO	Graphene oxide
Å	Angstrom
DMF	*N*,*N*-dimethylformamide

NMP	*N*-methylpyrrolidone
THF	Tetrahydrofuran
Zn^{2+}	Zinc (II) ions
GO-MPs	GO functionalised magnetic particles
CS/GO	Chitosan/graphene oxide
Au^{3+}	Gold (III) ions
Pd^{2+}	Lead (II) ions
MC/GO	Magnetic chitosan/graphene oxide
q_{eq}	Adsorbed amount at equilibrium
C_{eq}	Equilibrium concentration
T	Temperature
V_L	Volume
°C	Degrees Celsius
C_o	Initial concentration
m_A	mass
Δm^l	Mass removed from the liquid phase
Δm^a	Mass adsorbed onto the adsorbent
C	Mass concentration
q	Adsorbent loading
t	Time
q_m	Maximum adsorption capacity

b or K_L	Langmuir constant
g mol^{-1}	Grams per mole
Ca-Alg_2	Calcium alginate
Ca-Alg_2/GO	Calcium alginate/graphene oxide
h	Hour
%	Per cent
CPT	Camptothecin
DTAB	Dodecyltrimethylammonium bromide
BSA	Bovine serum albumin
$CaCl_2$	Calcium chloride
Na-Alg/HPMC	Sodium alginate/hydroxypropyl-methylcellulose
Na-Alg-g-PCL	Sodium alginate/poly(ε-caprolactone)
NaCMC	Sodium carboxymethyl cellulose
MAS	Magnesium aluminum silicate
MPs	Microspheres
AAM-g-HES	Acrylamide/hydroxyethyl cellulose
CDs	Cyclodextrins
α-CD	α-cyclodextrin
β-CD	β-cyclodextrin
γ-CD	γ-cyclodextrin
^{1}H NMR	^{1}H nuclear magnetic resonance

FTIR	Fourier transform infrared
TGA	Thermogravimetric analysis
XRD	X-ray diffraction
DSC	Differential scanning calorimetry
DBA	Dibenzalacetone
CLA	Crassicauline A
HP-β-CD	Hydroxypropyl-β-cyclodextrin
RDM-β-CD	Randomly substituted dimethyl-β-cyclodextrin
RDM-γ-CD	Randomly substituted dimethyl-γ-cyclodextrin
M, mol L^{-1}	Moles per litre
β-CD-*graft*-PAsp	β-cyclodextrin-grafted-α, β-poly (aspartic acid)
nm	Nanometer
mL	Millilitre
wt/wt %	Weight per weight per cent
g	Grams
min	Minute
mM	Millimolar
W	Weight
L	Litre
mg L^{-1}	Milligrams per litre
C_e	Final concentration

q_t	Adsorption capacity at time *t*
mg g^{-1}	Milligrams per gram
C_t	Concentration at time *t*
KBr	Potassium bromide
mL min^{-1}	Millilitres per minute
FIB/SEM	Focused ion beam scanning electron microscopy
cm	Centimeters
RB	Rose Bengal
Rubpy	Tris(2,2'-bipyridyl) dichlororuthenium (II) hexahydrate
DMSO	Dimethylsulfoxide
mm	millimeter
UV	Ultra violet
UV-vis	Ultra violet-visible
π	Pi
ATR-FTIR	Attenuated total reflection-Fourier transform infrared spectroscopy
β-CD-g-Alg	β–cyclodextrin-grafted-alginate
β-CD-6-OTs	Mono-6-deoxy-6-(*p*-toluenesulfonyl) β–cyclodextrin
Ts_2O	*ρ*-Toluenesulfonic anhydride
NH_4Cl	Ammonium chloride
TBA-Alg	Tetrabutylammonium-alginate

N	Normality
TBAOH	Tetrabutylammonium hydroxide
v/v	Volume per volume
δ	Chemical shifts
ppm	Parts per million
K_2	Rate constant of pseudo-second-order adsorption
C=O	Carbonyl
O-H	Hydroxyl
T_{max}	Maximum decomposition
T_i	Initial temperature
T_f	Final temperature
µM	Micrometer
g L^{-1}	Gram per litre
Chitosan-GLA	Chitosan-glutaraldehyde
R^2	Correlation coefficient
T_g	Glass transition temperature
R_{diff}	Diffusion rate
R_{relax}	Relaxation rate
M_t	Amounts of drug released at time *t*
M_∞	Amounts of drug released at infinite time
n	Release exponent

a	Scale parameter
b	Shape parameter
λ_{max}	Lambda maximum (wavelength)
H^+	Hydrogen ions
D	Diffusion coefficient
l	Thickness
s	Second
$-SO_2-O-$	Sulfonate
TBA^+	Tetrabutylammonium counterion
COO-	carboxyl group
D_2O	Deuterium oxide
d6-DMSO	Deuterated dimethylsulphoxide
CNBr	Cyanogen bromide
NR	Neutral red
x	Distance
Σ	Summation
HPMC	Hydroxypropylmethylcellulose
PVP	Polyvinylpyrrolidone
CMC	Carboxymethylcellulose
β-CD-dextrin	β-cyclodextrin-dextran
HC	Hydrocortisone

D_1	Diffusion coefficient for the fast release
D_2	Diffusion coefficient for the slow release
RF	Riboflavin
PLGA	Poly(lactide-*co*-glycolide)
PCL	Poly-ε-caprolactone
W/O/W	Water in oil in water
π	π is the ratio of a circle's circumference to its diameter (π = 3.1415)

Thesis guide

Objectives of the research

The main objectives of this thesis were to introduce methods for the preparation of an efficient material from sodium alginate for use as an adsorbent in water treatment and as a delivery vehicle in a drug delivery system. In order to achieve these objectives detailed descriptions of the milestones were as follows:

1- Calcium alginate (Ca-Alg_2) and calcium alginate with encapsulated graphene oxide (Ca-Alg_2/GO) gel bead adsorbents were fabricated. The ability of Ca-Alg_2 and Ca-Alg_2/GO gel beads to remove copper ions from aqueous solutions was investigated by varying the parameters; adsorbent doses, Cu^{2+} concentrations and contact times. The kinetic studies of the adsorption process were investigated.

2- The Ca-Alg_2 hydrogel was loaded with three different molecules; rose Bengal (RB), Tris(2,2'-bipyridyl) dichlororuthenium (II) hexahydrate (Rubpy) and camptothecin (CPT). Release of the three molecules from Ca-Alg_2 hydrogel at different pH's were monitored using UV-vis or fluorescence spectroscopies. The release mechanisms of RB, Rubpy and CPT from the Ca-Alg_2 hydrogels were studied using Ritger-Peppas and Weibull models. The diffusion coefficients of RB, Rubpy and CPT were determined using the Ritger-Peppas model.

3- β-cyclodextrin grafted sodium alginate (β-CD-g-Alg) was prepared and characterised. Subsequently, CPT inclusion complexes with β-CD (CPT/ β-CD) and β-CD-g-Alg (CPT/ β-CD-g-Alg) were fabricated and characterised using the a variety of scientific techniques such as attenuated total reflection-Fourier transform infrared (ATR-FTIR) and proton nuclear magnetic resonance (^{1}H NMR) spectroscopies.

4- The ability of the CPT/ β-CD-g-Alg inclusion complex in retarding the release of CPT was investigated and compared with the release of free CPT and CPT from CPT/ β-CD inclusion complexes. The diffusion coefficient values were then determined using Fick's second law.

Layout of thesis

This thesis consists of seven chapters wherein Chapter 1 describes the introduction of the polysaccharide polymer, sodium alginate and a literature review on Na-Alg as an adsorbent material in water treatment and as a delivery vehicle in drug delivery systems. The materials and the experimental procedures used throughout this thesis are described in Chapter 2. In this chapter, a brief description of the analytical instruments used throughout the studies is also given. Chapter 3 describes the preparation of Ca-Alg_2 and Ca-Alg_2/GO gel bead adsorbents, and their ability in the removal of Cu^{2+} ions from aqueous solutions is investigated. The release profiles of RB, Rubpy and CPT from the Ca-Alg_2 hydrogels are demonstrated in Chapter 4. Here the release mechanisms of RB, Rubpy and CPT are explained and the diffusion coefficients calculated. In Chapter 5, β-CD-g-Alg, CPT/ β-CD and CPT/ β-CD-g-Alg inclusion complexes are synthesised and characterised. In Chapter 6 the release profiles and the diffusion coefficients of CPT from CPT/ β-CD and CPT/ β-CD-g-Alg inclusion complexes were investigated. Chapter 7 concludes the previous chapters.