

# Application of Alginate in Water Treatment and Drug Delivery Systems



**Flinders**  
UNIVERSITY

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# Table of Contents

<b>Declaration.....</b>	<b>V</b>
<b>Acknowledgements.....</b>	<b>VI</b>
<b>Abstract.....</b>	<b>VIII</b>
<b>Publications.....</b>	<b>X</b>
<b>List of figures.....</b>	<b>XI</b>
<b>List of tables.....</b>	<b>XVI</b>
<b>List of abbreviations, symbols, and units.....</b>	<b>XVII</b>
<b>Thesis guide.....</b>	<b>XVII</b>
<b>Chapter 1. Introduction and literature review .....</b>	<b>1</b>
<b>1.1 Synopsis.....</b>	<b>1</b>
<b>1.2 Background on alginate .....</b>	<b>2</b>
1.2.1 Structure of sodium alginate (Na-Alg) .....	2
1.2.2 Production of Na-Alg.....	2
1.2.3 Physical properties of Na-Alg.....	4
1.2.4 Ionic cross-linking for gel formation .....	5
<b>1.3 Applications of calcium alginate (Ca-Alg<sub>2</sub>) ionotropic gels.....</b>	<b>11</b>
1.3.1 Ca-Alg <sub>2</sub> as an adsorbent in water treatment.....	11
1.3.2 Background on graphene.....	13
1.3.3 Graphite oxide and Graphene oxide (GO).....	14
1.3.4 Applications of GO.....	15
1.3.5 Adsorption technique.....	16
<b>1.4 Drug delivery systems .....</b>	<b>20</b>
1.4.1 Drug delivery systems based on hydrogels .....	23

1.4.2	Cyclodextrins (CDs) for improved drug delivery systems .....	26
1.4.3	$\beta$ -cyclodextrin grafted polymers as drug delivery system.....	31
<b>1.5</b>	<b>Summary.....</b>	<b>33</b>
<b>Chapter 2.</b>	<b>Experimental.....</b>	<b>34</b>
<b>2.1</b>	<b>Synopsis.....</b>	<b>34</b>
<b>2.2</b>	<b>Materials .....</b>	<b>35</b>
2.2.1	Chemicals and reagents.....	35
<b>2.3</b>	<b>Polymer solution preparation.....</b>	<b>37</b>
2.3.1	Sodium alginate (Na-Alg) solution.....	37
2.3.2	Sodium alginate / graphene oxide (Na-Alg/GO) solution .....	37
2.3.3	Na-Alg and Na-Alg/GO solutions storage.....	38
<b>2.4</b>	<b>Iontropic gel beads synthesis .....</b>	<b>38</b>
2.4.1	Calcium alginate (Ca-Alg <sub>2</sub> ) ionotropic gel beads .....	38
2.4.2	Calcium alginate/graphene oxide (Ca-Alg <sub>2</sub> /GO) ionotropic gel beads .....	39
<b>2.5</b>	<b>Batch Cu<sup>2+</sup> ion adsorption experiments .....</b>	<b>40</b>
2.5.1	Preparation of electrolyte solutions .....	40
2.5.2	Effect of initial copper concentration .....	40
2.5.3	Effect of adsorbent dose on Cu <sup>2+</sup> ion adsorption.....	41
<b>2.6</b>	<b>Kinetic experiments.....</b>	<b>42</b>
<b>2.7</b>	<b>Adsorbent characterisation techniques.....</b>	<b>42</b>
2.7.1	Fourier transform infrared (FT-IR) spectroscopy .....	42
2.7.2	Thermogravimetric analysis (TGA).....	43
2.7.3	Focused ion beam scanning electron microscopy (FIB/SEM).....	43
<b>2.8</b>	<b>Drug delivery.....</b>	<b>44</b>
2.8.1	Fabrication of Ca-Alg <sub>2</sub> hydrogel membranes .....	44
2.8.2	Loading rose Bengal (RB) or Rubpy or camptothecin (CPT) into Ca-Alg <sub>2</sub> hydrogel membranes.....	45
<b>2.9</b>	<b>Release of RB or Rubpy or CPT from Ca-Alg<sub>2</sub> hydrogel membranes.....</b>	<b>46</b>
2.9.1	Ultra-Violet-Visible (UV-Vis) spectrophotometry.....	47
2.9.2	Fluorescence spectrophotometry .....	47
<b>2.10</b>	<b>Hydrogel disc characterisation techniques.....</b>	<b>48</b>
2.10.1	Scanning electron microscopy (SEM) .....	48
<b>2.11</b>	<b>CPT/<math>\beta</math>-CD and CPT/<math>\beta</math>-CD-g-Alg inclusion complexes synthesis.....</b>	<b>49</b>
2.11.1	Preparation of Camptothecin/ $\beta$ -cyclodextrin (CPT/ $\beta$ -CD) inclusion complex	49

2.11.2	Preparation of camptothecin / $\beta$ -cyclodextrin-grafted-alginate (CPT/ $\beta$ -CD-g-Alg) inclusion complex.....	49
<b>2.12</b>	<b>CPT release experiment .....</b>	<b>51</b>
<b>2.13</b>	<b>Inclusion complexes characterisation techniques.....</b>	<b>51</b>
2.13.1	Fourier transform infrared spectroscopy.....	51
2.13.2	$^1\text{H}$ nuclear magnetic resonance spectroscopy .....	52
2.13.3	Thermogravimetric analysis (TGA).....	52
<b>Chapter 3.</b>	<b>Alginate-grahene oxide hybrid gel beads: An efficient copper adsorbent material.....</b>	<b>53</b>
<b>3.1</b>	<b>Synopsis.....</b>	<b>53</b>
<b>3.2</b>	<b>Introduction.....</b>	<b>54</b>
3.2.1	Adsorption isotherm modelling.....	54
3.2.2	Adsorption kinetic modelling .....	54
<b>3.3</b>	<b>Synthesis and characterisation of Ca-Alg<sub>2</sub> and Ca-Alg<sub>2</sub>/GO ionotropic beads.....</b>	<b>55</b>
<b>3.4</b>	<b>Characterisation of Ca-Alg<sub>2</sub> and Ca-Alg<sub>2</sub>/GO ionotropic beads.....</b>	<b>55</b>
3.4.1	FT-IR spectroscopy characterisation of Ca-Alg <sub>2</sub> ionotropic beads .....	55
3.4.2	TGA analysis of Ca-Alg <sub>2</sub> and Ca-Alg <sub>2</sub> /GO beads.....	57
3.4.3	FIB/SEM analysis of Ca-Alg <sub>2</sub> and Ca-Alg <sub>2</sub> /GO beads.....	59
<b>3.5</b>	<b>Copper adsorption studies of Ca-Alg<sub>2</sub> and Ca-Alg<sub>2</sub>/GO gel beads .....</b>	<b>60</b>
3.5.1	Effect of adsorbent dose (batch experiments) .....	61
3.5.2	Effect of copper ion concentrations .....	63
<b>3.6</b>	<b>Effect of contact time .....</b>	<b>66</b>
3.6.1	Adsorption kinetics .....	66
<b>3.7</b>	<b>Concluding remarks.....</b>	<b>72</b>
<b>Chapter 4.</b>	<b>Study of dye and anticancer drug release from calcium alginate hydrogels.....</b>	<b>74</b>
<b>4.1</b>	<b>Synopsis.....</b>	<b>74</b>
<b>4.2</b>	<b>Introduction.....</b>	<b>75</b>
4.2.1	Diffusion models.....	76
<b>4.3</b>	<b>Properties of RB, Rubpy and CPT .....</b>	<b>78</b>
<b>4.4</b>	<b>Release profile of RB, Rubpy, and CPT from Ca-Alg<sub>2</sub> hydrogel .....</b>	<b>79</b>
4.4.1	RB and Rubpy release measured by UV-Vis spectroscopy.....	80
4.4.2	CPT release measured by fluorescence spectroscopy.....	83
<b>4.5</b>	<b>Diffusion kinetics .....</b>	<b>85</b>

4.5.1	Fractional amount of RB, Rubpy and CPT release.....	85
<b>4.6</b>	<b>Release kinetics.....</b>	<b>92</b>
<b>4.7</b>	<b>Concluding remarks.....</b>	<b>98</b>
<b>Chapter 5.</b>	<b>CPT/ <math>\beta</math>-CD and CPT/<math>\beta</math>-CD-g-Alg Inclusion complexes</b>	
	<b>fabrication and characterisation .....</b>	<b>100</b>
<b>5.1</b>	<b>Synopsis.....</b>	<b>100</b>
<b>5.2</b>	<b>Synthesis and characterisation of <math>\beta</math>-CD-6-OTs.....</b>	<b>101</b>
5.2.1	ATR-FTIR spectroscopic characterisation of $\beta$ -CD-6-OTs.....	103
<b>5.3</b>	<b>Synthesis and characterisation of TBA-Alg.....</b>	<b>103</b>
5.3.1	ATR-FTIR spectroscopic characterisation of TBA-Alg.....	104
<b>5.4</b>	<b>Synthesis and characterisation of <math>\beta</math>-CD-g-Alg .....</b>	<b>105</b>
5.4.1	ATR-FTIR spectroscopic characterisation of $\beta$ -CD-g-Alg.....	105
<b>5.5</b>	<b>Synthesis and characterisation of CPT/<math>\beta</math>-CD and CPT/<math>\beta</math>-CD-g-Alg inclusion</b>	
	<b>complexes.....</b>	<b>106</b>
5.5.1	Characterisation of CPT/ $\beta$ -CD inclusion complexes .....	107
5.5.2	Characterisation of CPT/ $\beta$ -CD-g-Alg complexes.....	114
<b>5.6</b>	<b>Concluding remarks.....</b>	<b>123</b>
<b>Chapter 6.</b>	<b>Study of Camptothecin release from CPT/<math>\beta</math>-CD and CPT/<math>\beta</math>-CD-</b>	
	<b>g-Alg inclusion complexes .....</b>	<b>124</b>
<b>6.1</b>	<b>Synopsis.....</b>	<b>124</b>
<b>6.2</b>	<b>Introduction.....</b>	<b>125</b>
<b>6.3</b>	<b>Diffusion coefficient modelling.....</b>	<b>126</b>
<b>6.4</b>	<b>Fractional amount of CPT release .....</b>	<b>127</b>
6.4.1	CPT release measured by UV-Vis spectroscopy.....	128
6.4.2	Fractional amount of free CPT release and CPT release from CPT/ $\beta$ -CD and	
	CPT/ $\beta$ -CD-g-Alg inclusion complexes.....	130
<b>6.5</b>	<b>Diffusion coefficient of CPT release .....</b>	<b>133</b>
6.5.1	Fitting Fick's second law .....	133
6.5.2	Release diffusion coefficients.....	135
<b>6.6</b>	<b>Concluding remarks.....</b>	<b>138</b>
<b>Chapter 7.</b>	<b>Conclusions and recommendations .....</b>	<b>139</b>
<b>7.1</b>	<b>Synopsis.....</b>	<b>139</b>
<b>7.2</b>	<b>Conclusions .....</b>	<b>140</b>
<b>7.3</b>	<b>Recommendations.....</b>	<b>143</b>

<b>References</b>	<b>145</b>
<b>Appendices</b>	<b>i</b>

# 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<sub>2</sub> hydrogels in water treatment and drug delivery system. Ca-Alg<sub>2</sub> and Ca-Alg<sub>2</sub>/GO gel bead adsorbents fabricated for the removal of Cu<sup>2+</sup> ions from aqueous solution. The influence of the use of different adsorbent doses, Cu<sup>2+</sup> 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<sub>2</sub>.

Chapter two discusses the loading of RB, Rubpy and CPT into Ca-Alg<sub>2</sub> 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<sub>2</sub> hydrogel. The molecular weight and the charge of the dye or drug play an important role in the release process from Ca-Alg<sub>2</sub> 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  $\beta$ -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/ $\beta$ -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/ $\beta$ -CD inclusion complex and enhanced the formation of CPT/ $\beta$ -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.

# List of Figures

Figure 1-1 Alginate composition. (a) $\beta$ -D-mannuronic acid, (b) $\alpha$ -L-guluronic acid and (c) various structural formulae of sodium alginate [1].	2
Figure 1-2 Schematic diagram of the typical extraction process of sodium alginate from brown algae [4].	<b>Error! Bookmark not defined.</b>
Figure 1-3 Binding of divalent cations by alginate (Egg-box) model [1].	6
Figure 1-4 Schematic structure of G-alginate junction zone. (a) $\text{Ca}^{2+}$ (blue dots) located along the chain axis and $\text{Na}^+$ or $\text{Ca}^{2+}$ (red dots) located between alginate dimers that pack through unspecific interactions and (b) long-range $\text{Ca}^{2+}$ located between interacting chains [18].	7
Figure 1-5 Intramolecular (left) and intermolecular (right) geometrical structures of divalent metal alginate ionotropic complexes [19].	8
Figure 1-6 Intermolecular geometrical structure of a trivalent metal ionotropic alginate complex [11].	8
Figure 1-7 Depiction of two fundamental methods for preparing alginate gel. (a) the diffusion or external method and (b) the internal method [9].	10
Figure 1-8 Structures of the different allotropes of carbon [44].	13
Figure 1-9 A proposed chemical structure of graphene oxide [52].	15
Figure 1-10 Adsorption isotherm [62].	17
Figure 1-11 Determination of equilibrium data [62].	18
Figure 1-12 Drug release profile (a) traditional drug delivery systems and (b) controlled release systems [71].	22
Figure 1-13 Schematic illustration of hydrophobically modified biomineralised polysaccharide alginate membrane [73].	22
Figure 1-14 Chemical structure of camptothecin and equilibrium reaction between the active lactone form and the inactive carboxylate form [85].	24
Figure 1-15 Structure of cyclodextrins [106].	26
Figure 1-16 Structure of the inclusion complex [108].	27
Figure 1-17 3D structural representation of (a) $\beta$ -CD, (b) DBA and (c) $\beta$ -CD/DBA inclusion complex [110].	28
Figure 1-18 Possible $\beta$ -CD/CLA inclusion complex mode [112].	29

Figure 1-19 Schematic representation of the 2:1 inclusion complexes (a) 2:1 inclusion complexes from pure $\beta$ -CD and (b) 2:1 inclusion complexes from $\beta$ -CD polymer [116].....	31
Figure 1-20 Synthesis scheme of $\beta$ -CD-graft-PAsp [115].....	32
Figure 1-21 Synthesis scheme of mPEG-PLG(CD) [103].....	32
Figure 2-1 Images of aqueous solutions of (a) Na-Alg and (b) Na-Alg/GO. ....	38
Figure 2-2 Images of (a) Ca-Alg <sub>2</sub> and (b) Ca-Alg <sub>2</sub> /GO wet gel beads. ....	40
Figure 2-3 Images of Ca-Alg <sub>2</sub> cylindrical hydrogel. ....	45
Figure 2-4 Optical images of (a) pure Ca-Alg <sub>2</sub> hydrogel, (b) Ca-Alg <sub>2</sub> hydrogel loaded with RB, (c) Ca-Alg <sub>2</sub> hydrogel loaded with Rubpy and (d) Ca-Alg <sub>2</sub> hydrogel loaded with CPT. ....	46
Figure 3-1 FT-IR spectrum of (a) GO, (b) Ca-Alg <sub>2</sub> and (c) Ca-Alg <sub>2</sub> /GO gel beads. ....	56
Figure 3-2 TGA thermograms of (a) Ca-Alg <sub>2</sub> and (b) Ca-Alg <sub>2</sub> /GO beads. ....	58
Figure 3-3 FIB/SEM images of (a) Ca-Alg <sub>2</sub> and (b) Ca-Alg <sub>2</sub> /GO gel beads after drying in molten naphthalene. Circled image in (b) indicates more defined porous structure in Ca-Alg <sub>2</sub> /GO. ....	60
Figure 3-4 The effect of adsorbent dose on the adsorption of Cu <sup>2+</sup> ions using Ca-Alg <sub>2</sub> (Initial Cu <sup>2+</sup> ion concentration = 635 mg L <sup>-1</sup> , contact time = 90 min).....	62
Figure 3-5 The effect of adsorbent dose on the adsorption of Cu <sup>2+</sup> ions using Ca-Alg <sub>2</sub> /GO. (Initial Cu <sup>2+</sup> ion concentration = 635 mg L <sup>-1</sup> , contact time = 90 min). ....	63
Figure 3-6 Adsorption isotherm of copper ion onto 100 beads of (a) Ca-Alg <sub>2</sub> with an adsorbent dose of 0.29 g L <sup>-1</sup> (b) Ca-Alg <sub>2</sub> /GO with an adsorbent dose of 0.26 g L <sup>-1</sup> , and contact time = 90 min and solution volume =150 mL. Shapes represent experimental data, while solid lines represent Langmuir modelling results.....	64
Figure 3-7 Langmuir model adsorption isotherm plot of Cu <sup>2+</sup> ions adsorption onto 100 beads of (a) Ca-Alg <sub>2</sub> with an adsorbent dose of 0.29 g L <sup>-1</sup> and (b) Ca-Alg <sub>2</sub> /GO with an adsorbent dose of 0.26 g L <sup>-1</sup> , and contact time = 90 min and solution volume = 150 mL.....	65
Figure 3-8 Effect of contact time on the Cu <sup>2+</sup> ion adsorption of 100 gel beads (a) Ca-Alg <sub>2</sub> (0.29 g L <sup>-1</sup> of adsorbent) (b) Ca-Alg <sub>2</sub> /GO (0.26 g L <sup>-1</sup> of adsorbent) and a solution volume = 15 mL, at a Cu <sup>2+</sup> ion concentrations of (i) 317 mg L <sup>-1</sup> , (ii) 476 mg L <sup>-1</sup> and (iii) 635 mg L <sup>-1</sup> . ....	68
Figure 3-9 Pseudo-second-order kinetic plots for the adsorption of Cu <sup>2+</sup> ions on (a) Ca-Alg <sub>2</sub> (0.29 g L <sup>-1</sup> of adsorbent) and (b) Ca-Alg <sub>2</sub> /GO (0.26 g L <sup>-1</sup> of adsorbent) gel	

beads and a solution volume = 15 mL, at a  $\text{Cu}^{2+}$  ion concentrations of (i)  $317 \text{ mg L}^{-1}$ , (ii)  $476 \text{ mg L}^{-1}$  and (iii)  $635 \text{ mg L}^{-1}$ . Lines represent the fitting data to equation 3.2. .... 70

Figure 4-1 UV-Vis spectra of Tris buffer solution at pH ~ 7.4 in the release experiment of RB from Ca-Alg<sub>2</sub> hydrogel discs..... 81

Figure 4-2 UV-Vis spectra of Tris buffer solution at pH ~ 2.4 in the release experiment of Rubpy from Ca-Alg<sub>2</sub> hydrogel discs. .... 81

Figure 4-3 UV-Vis spectra of Tris buffer solution at pH ~ 7.4 in the release experiment of Rubpy from Ca-Alg<sub>2</sub> hydrogel discs. .... 82

Figure 4-4 Change in concentration of RB and Rubpy in Tris buffer solution at pH ~2.4 and pH ~ 7.4 in the release experiment of RB and Rubpy from a Ca-Alg<sub>2</sub> hydrogel disc..... 82

Figure 4-5 Fluorescence emission spectra at an excitation wavelength of 370 nm of the Tris buffer solution at pH ~ 2.4 in the release experiment of CPT (lactone form) from a Ca-Alg<sub>2</sub> hydrogel disc. .... 83

Figure 4-6 Fluorescence emission spectra at an excitation wavelength of 370 nm of the Tris buffer solution at pH ~ 7.4 in the release experiment of CPT (carboxylate form) from a Ca-Alg<sub>2</sub> hydrogel disc. .... 84

Figure 4-7 Change in concentration of CPT in Tris buffer solution at pH ~ 2.4 and pH ~ 7.4 in the release experiment of CPT from a Ca-Alg<sub>2</sub> hydrogel disc. .... 84

Figure 4-8 Fraction release,  $M_t/M_\infty$  of Rubpy (black squares) and CPT (red triangles) from Ca-Alg<sub>2</sub> hydrogel discs at pH ~ 2.4..... 85

Figure 4-9 Optical images of (a) a dried pure Ca-Alg<sub>2</sub> disc, (b) a dried Ca-Alg<sub>2</sub> disc loaded with CPT after 103 min in pH ~ 2.4 and (c) a dried Ca-Alg<sub>2</sub> disc loaded with CPT after 103 min in pH ~ 7.4 ..... 87

Figure 4-10 SEM images of (a) a dried Ca-Alg<sub>2</sub> disc, (b) a dried Ca-Alg<sub>2</sub> disc loaded with CPT after 103 min in pH ~ 2.4 and (c) a dried Ca-Alg<sub>2</sub> disc loaded with CPT after 103 min in pH ~ 7.4..... 88

Figure 4-11 Fraction release,  $M_t/M_\infty$  of RB (green circles), Rubpy (black squares) and CPT (red triangles) from Ca-Alg<sub>2</sub> discs at pH ~ 7.4..... 90

Figure 4-12 Ritger-Peppas model of RB (green circles), Rubpy (black squares) and CPT (red triangles), (a) at pH ~ 2.4 and (b) at pH ~ 7.4..... 93

Figure 4-13 Weibull model of RB (green circles), Rubpy (black squares) and CPT (red triangles), (a) at pH ~ 2.4 and (b) at pH ~ 7.4. ....	96
Figure 5-1 Synthesis of $\beta$ -cyclodextrin grafted sodium alginate [127]. ....	102
Figure 5-2 ATR-FTIR spectra of (a) $\beta$ -CD and (b) $\beta$ -CD-6-OTs. ....	103
Figure 5-3 ATR-FTIR spectra of (a) Na-Alg and (b) TBA-Alg. ....	105
Figure 5-4 ATR-FTIR spectra of (a) $\beta$ -CD-6-OTs, (b) TBA-Alg and (c) $\beta$ -CD-g-Alg. ....	106
Figure 5-5 ATR-FTIR spectra of (a) $\beta$ -CD, (b) CPT and (c) a CPT/ $\beta$ -CD inclusion complex. ....	108
Figure 5-6 $^1\text{H}$ NMR spectroscopy spectra of (a) $\beta$ -CD and (b) a CPT/ $\beta$ -CD inclusion complexes. ....	110
Figure 5-7 Simplified model of CPT/ $\beta$ -CD inclusion complex, (Note: OH groups not represented on the $\beta$ -CD). ....	110
Figure 5-8 TGA thermograms of (a) CPT, (b) $\beta$ -CD and (c) CPT/ $\beta$ -CD. ....	113
Figure 5-9 ATR-FTIR spectra of (a) $\beta$ -CD-g-Alg, (b) CPT and (c) CPT/ $\beta$ -CD-g-Alg inclusion complex. ....	115
Figure 5-10 $^1\text{H}$ NMR spectra of $\beta$ -CD-g-Alg. ....	117
Figure 5-11 $^1\text{H}$ NMR spectra of a CPT/ $\beta$ -CD-g-Alg inclusion complex. ....	118
Figure 5-12 TGA thermograms of (a) CPT, (b) $\beta$ -CD and (c) Na-Alg and (d) CPT/ $\beta$ -CD-g-Alg inclusion complex. ....	121
Figure 6-1 UV-Vis spectra of Tris buffer solution at pH ~ 7.4 and at 37 °C in the release experiment of free CPT from a dialysis membrane. ....	129
Figure 6-2 UV-Vis spectra of Tris buffer solution at pH ~ 7.4 and at 37 °C in the release experiment of CPT from the CPT/ $\beta$ -CD inclusion complex. ....	129
Figure 6-3 UV-Vis spectra of Tris buffer solution at pH ~ 7.4 and at 37 °C in the release experiment of CPT from CPT/ $\beta$ -CD-g-Alg inclusion complex. ....	130
Figure 6-4 Fraction release, $M_t/M_\infty$ of free CPT (red circles), CPT from CPT/ $\beta$ -CD inclusion complex (black circles) and CPT from CPT/ $\beta$ -CD-g-Alg inclusion complex (blue circles). Insert: Fraction release, $M_t/M_\infty$ of CPT from Ca-Alg <sub>2</sub> hydrogel discs at pH ~ 7.4. ....	131
Figure 6-5 Semi-logarithmic plots of the data in Figure 6.4 as a function of time for free CPT (red circles) and CPT from CPT/ $\beta$ -CD inclusion complex (black circles), (a) is a first stage (fast release) and (b) is a second stage (slow release). ....	134



Figure 6-6 Semi-logarithmic plot of the data in Figure 6.4 as a function of time for CPT from a CPT/ $\beta$ -CD-g-Alg inclusion complex. ....	135
Figure 1 Calibration curve for $\text{Cu}^{2+}$ ions. ....	i
Figure 2 Calibration curves of (a) RB, (b) Rubpy and (c) CPT.....	ii
Figure 3 Calibration curves of CPT.....	iii

## List of tables

Table 2-1 Chemicals and reagents. ....	35
Table 3-1 The maximum decomposition ( $T_{\max}$ ) and the weight loss accompanying to the stages decomposition. ....	59
Table 3-2 Langmuir isotherm constants and correlation coefficient of $\text{Cu}^{2+}$ adsorption onto 100 beads of $\text{Ca-Alg}_2$ and $\text{Ca-Alg}_2/\text{GO}$ with adsorbent dose of $0.29 \text{ g L}^{-1}$ and $0.26 \text{ g L}^{-1}$ , respectively, contact time: 90 min and volume of solution: 150 mL.....	66
Table 3-3 The equilibrium adsorption capacity ( $q_e$ ), the rate constant ( $K_2$ ) and the correlation coefficients ( $R^2$ ) of the pseudo-second-order kinetic for $\text{Cu}^{2+}$ ion adsorption onto $\text{Ca-Alg}_2$ and $\text{Ca-Alg}_2/\text{GO}$ gel beads.....	71
Table 4-1 Properties of the RB, Rubpy and CPT [84, 159-161]. ....	78
Table 4-2 Ritger-Peppas and Weibull model parameters with correlation coefficients for RB, Rubpy and CPT release from $\text{Ca-Alg}_2$ hydrogel disc at $\text{pH} \sim 2.4$ and $\text{pH} \sim 7.4$ . ....	94
Table 5-1 $^1\text{H}$ NMR chemical shifts ( $\delta$ /ppm) for the protons of $\beta$ -CD (free) and CPT/ $\beta$ -CD (complex) inclusion complex. ....	111
Table 5-2 The $T_i$ and $T_f$ decomposition temperatures ( $^\circ\text{C}$ ) as well as the weight loss accompanying the stage of decomposition for CPT, $\beta$ -CD and CPT/ $\beta$ -CD .....	114
Table 5-3 $^1\text{H}$ NMR chemical shifts ( $\delta$ /ppm) for the protons of CPT (free) and CPT/ $\beta$ -CD-g-Alg inclusion complex (complex). ....	119
Table 5-4 The $T_i$ and $T_f$ decomposition temperatures ( $^\circ\text{C}$ ) as well as the weight loss accompanying each stage of decomposition for Na-Alg and CPT/ $\beta$ -CD-g-Alg inclusion complex. ....	122
Table 6-1 The release diffusion coefficients of free CPT and CPT from the CPT/ $\beta$ -CD and CPT/ $\beta$ -CD-g-Alg inclusion complexes in Tris buffer. ....	136

## Lists of abbreviations, symbols and units

<b>Symbol/acronym/unit</b>	<b>Translation/explanation</b>
<b>Na-Alg</b>	Sodium alginate
<b>H-Alg</b>	Alginic acid
<b>G</b>	Guluronic
<b>GDL</b>	D-glucono- $\delta$ -lactone
<b>M</b>	Mannuronic
<b>Ca<sup>2+</sup></b>	Calcium (II) ions
<b>Sr<sup>2+</sup></b>	Strontium (II) ions
<b>Ba<sup>2+</sup></b>	Barium (II) ions
<b>pH</b>	Power of Hydrogen (per Hydrogen)
<b>pK<sub>a</sub></b>	Acidic constant
<b>Cu<sup>2+</sup></b>	Copper (II) ions
<b>Ni<sup>2+</sup></b>	Nickel (II) ions
<b>Co<sup>2+</sup></b>	Cobalt (II) ions
<b>CaCO<sub>3</sub></b>	Calcium carbonate
<b>Na<sup>+</sup></b>	Sodium (I) ions
<b>CNTs</b>	Carbon nanotubes
<b>GO</b>	Graphene oxide
<b>Å</b>	Angstrom
<b>DMF</b>	<i>N,N</i> -dimethylformamide

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<b>NMP</b>	<i>N</i> -methylpyrrolidone
<b>THF</b>	Tetrahydrofuran
<b>Zn<sup>2+</sup></b>	Zinc (II) ions
<b>GO-MPs</b>	GO functionalised magnetic particles
<b>CS/GO</b>	Chitosan/graphene oxide
<b>Au<sup>3+</sup></b>	Gold (III) ions
<b>Pd<sup>2+</sup></b>	Lead (II) ions
<b>MC/GO</b>	Magnetic chitosan/graphene oxide
<b><i>q<sub>eq</sub></i></b>	Adsorbed amount at equilibrium
<b><i>C<sub>eq</sub></i></b>	Equilibrium concentration
<b>T</b>	Temperature
<b><i>V<sub>L</sub></i></b>	Volume
<b>°C</b>	Degrees Celsius
<b><i>C<sub>0</sub></i></b>	Initial concentration
<b><i>m<sub>A</sub></i></b>	mass
<b><math>\Delta m^l</math></b>	Mass removed from the liquid phase
<b><math>\Delta m^a</math></b>	Mass adsorbed onto the adsorbent
<b><i>C</i></b>	Mass concentration
<b><i>q</i></b>	Adsorbent loading
<b>t</b>	Time
<b><i>q<sub>m</sub></i></b>	Maximum adsorption capacity

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<b><i>b or K<sub>L</sub></i></b>	Langmuir constant
<b><i>g mol<sup>-1</sup></i></b>	Grams per mole
<b>Ca-Alg<sub>2</sub></b>	Calcium alginate
<b>Ca-Alg<sub>2</sub>/GO</b>	Calcium alginate/graphene oxide
<b>h</b>	Hour
<b>%</b>	Per cent
<b>CPT</b>	Camptothecin
<b>DTAB</b>	Dodecyltrimethylammonium bromide
<b>BSA</b>	Bovine serum albumin
<b>CaCl<sub>2</sub></b>	Calcium chloride
<b>Na-Alg/HPMC</b>	Sodium alginate/hydroxypropyl-methylcellulose
<b>Na-Alg-g-PCL</b>	Sodium alginate/poly( $\epsilon$ -caprolactone)
<b>NaCMC</b>	Sodium carboxymethyl cellulose
<b>MAS</b>	Magnesium aluminum silicate
<b>MPs</b>	Microspheres
<b>AAM-g-HES</b>	Acrylamide/hydroxyethyl cellulose
<b>CDs</b>	Cyclodextrins
<b><math>\alpha</math>-CD</b>	$\alpha$ -cyclodextrin
<b><math>\beta</math>-CD</b>	$\beta$ -cyclodextrin
<b><math>\gamma</math>-CD</b>	$\gamma$ -cyclodextrin
<b><sup>1</sup>H NMR</b>	<sup>1</sup> H nuclear magnetic resonance

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<b>FTIR</b>	Fourier transform infrared
<b>TGA</b>	Thermogravimetric analysis
<b>XRD</b>	X-ray diffraction
<b>DSC</b>	Differential scanning calorimetry
<b>DBA</b>	Dibenzalacetone
<b>CLA</b>	Crassicauline A
<b>HP-<math>\beta</math>-CD</b>	Hydroxypropyl- $\beta$ -cyclodextrin
<b>RDM-<math>\beta</math>-CD</b>	Randomly substituted dimethyl- $\beta$ -cyclodextrin
<b>RDM-<math>\gamma</math>-CD</b>	Randomly substituted dimethyl- $\gamma$ -cyclodextrin
<b>M, mol L<sup>-1</sup></b>	Moles per litre
<b><math>\beta</math>-CD-<i>graft</i>-PAsp</b>	$\beta$ -cyclodextrin-grafted- $\alpha$ , $\beta$ -poly (aspartic acid)
<b>nm</b>	Nanometer
<b>mL</b>	Millilitre
<b>wt/wt %</b>	Weight per weight per cent
<b>g</b>	Grams
<b>min</b>	Minute
<b>mM</b>	Millimolar
<b>W</b>	Weight
<b>L</b>	Litre
<b>mg L<sup>-1</sup></b>	Milligrams per litre
<b>C<sub>e</sub></b>	Final concentration

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$q_t$	Adsorption capacity at time $t$
$\text{mg g}^{-1}$	Milligrams per gram
$C_t$	Concentration at time $t$
<b>KBr</b>	Potassium bromide
$\text{mL min}^{-1}$	Millilitres per minute
<b>FIB/SEM</b>	Focused ion beam scanning electron microscopy
<b>cm</b>	Centimeters
<b>RB</b>	Rose Bengal
<b>Rubpy</b>	Tris(2,2'-bipyridyl) dichlororuthenium (II) hexahydrate
<b>DMSO</b>	Dimethylsulfoxide
<b>mm</b>	millimeter
<b>UV</b>	Ultra violet
<b>UV-vis</b>	Ultra violet-visible
$\pi$	Pi
<b>ATR-FTIR</b>	Attenuated total reflection-Fourier transform infrared spectroscopy
<b><math>\beta</math>-CD-g-Alg</b>	$\beta$ -cyclodextrin-grafted-alginate
<b><math>\beta</math>-CD-6-OTs</b>	Mono-6-deoxy-6-( <i>p</i> -toluenesulfonyl) $\beta$ -cyclodextrin
<b>Ts<sub>2</sub>O</b>	<i>p</i> -Toluenesulfonic anhydride
<b>NH<sub>4</sub>Cl</b>	Ammonium chloride
<b>TBA-Alg</b>	Tetrabutylammonium-alginate

<b>N</b>	Normality
<b>TBAOH</b>	Tetrabutylammonium hydroxide
<b>v/v</b>	Volume per volume
<b>δ</b>	Chemical shifts
<b>ppm</b>	Parts per million
<b>K<sub>2</sub></b>	Rate constant of pseudo-second-order adsorption
<b>C=O</b>	Carbonyl
<b>O-H</b>	Hydroxyl
<b>T<sub>max</sub></b>	Maximum decomposition
<b>T<sub>i</sub></b>	Initial temperature
<b>T<sub>f</sub></b>	Final temperature
<b>μM</b>	Micrometer
<b>g L<sup>-1</sup></b>	Gram per litre
<b>Chitosan-GLA</b>	Chitosan-glutaraldehyde
<b>R<sup>2</sup></b>	Correlation coefficient
<b>T<sub>g</sub></b>	Glass transition temperature
<b>R<sub>diff</sub></b>	Diffusion rate
<b>R<sub>relax</sub></b>	Relaxation rate
<b>M<sub>t</sub></b>	Amounts of drug released at time <i>t</i>
<b>M<sub>∞</sub></b>	Amounts of drug released at infinite time
<b>n</b>	Release exponent



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<i>a</i>	Scale parameter
<i>b</i>	Shape parameter
$\lambda_{\max}$	Lambda maximum (wavelength)
$H^+$	Hydrogen ions
<i>D</i>	Diffusion coefficient
<i>l</i>	Thickness
<i>s</i>	Second
<b>-SO<sub>2</sub>-O-</b>	Sulfonate
<b>TBA<sup>+</sup></b>	Tetrabutylammonium counterion
<b>COO-</b>	carboxyl group
<b>D<sub>2</sub>O</b>	Deuterium oxide
<b>d6-DMSO</b>	Deuterated dimethylsulphoxide
<b>CNBr</b>	Cyanogen bromide
<b>NR</b>	Neutral red
<i>x</i>	Distance
$\Sigma$	Summation
<b>HPMC</b>	Hydroxypropylmethylcellulose
<b>PVP</b>	Polyvinylpyrrolidone
<b>CMC</b>	Carboxymethylcellulose
<b><math>\beta</math>-CD-dextrin</b>	$\beta$ -cyclodextrin-dextran
<b>HC</b>	Hydrocortisone

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<b>D<sub>1</sub></b>	Diffusion coefficient for the fast release
<b>D<sub>2</sub></b>	Diffusion coefficient for the slow release
<b>RF</b>	Riboflavin
<b>PLGA</b>	Poly(lactide- <i>co</i> -glycolide)
<b>PCL</b>	Poly- $\epsilon$ -caprolactone
<b>W/O/W</b>	Water in oil in water
<b><math>\pi</math></b>	$\pi$ is the ratio of a circle's circumference to its diameter ( $\pi = 3.1415$ )

# 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<sub>2</sub>) and calcium alginate with encapsulated graphene oxide (Ca-Alg<sub>2</sub>/GO) gel bead adsorbents were fabricated. The ability of Ca-Alg<sub>2</sub> and Ca-Alg<sub>2</sub>/GO gel beads to remove copper ions from aqueous solutions was investigated by varying the parameters; adsorbent doses, Cu<sup>2+</sup> concentrations and contact times. The kinetic studies of the adsorption process were investigated.
- 2- The Ca-Alg<sub>2</sub> hydrogel was loaded with three different molecules; rose Bengal (RB), Tris(2,2'-bipyridyl) dichlororuthenium (II) hexahydrate (Rbpy) and camptothecin (CPT). Release of the three molecules from Ca-Alg<sub>2</sub> hydrogel at different pH's were monitored using UV-vis or fluorescence spectroscopies. The release mechanisms of RB, Rbpy and CPT from the Ca-Alg<sub>2</sub> hydrogels were studied using Ritger-Peppas and Weibull models. The diffusion coefficients of RB, Rbpy and CPT were determined using the Ritger-Peppas model.
- 3-  $\beta$ -cyclodextrin grafted sodium alginate ( $\beta$ -CD-g-Alg) was prepared and characterised. Subsequently, CPT inclusion complexes with  $\beta$ -CD (CPT/  $\beta$ -CD) and  $\beta$ -CD-g-Alg (CPT/  $\beta$ -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 (<sup>1</sup>H NMR) spectroscopies.

- 4- The ability of the CPT/  $\beta$ -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/  $\beta$ -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<sub>2</sub> and Ca-Alg<sub>2</sub>/GO gel bead adsorbents, and their ability in the removal of Cu<sup>2+</sup> ions from aqueous solutions is investigated. The release profiles of RB, Rubpy and CPT from the Ca-Alg<sub>2</sub> 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](#),  $\beta$ -CD-g-Alg, CPT/  $\beta$ -CD and CPT/  $\beta$ -CD-g-Alg inclusion complexes are synthesised and characterised. In Chapter 6 the release profiles and the diffusion coefficients of CPT from CPT/  $\beta$ -CD and CPT/  $\beta$ -CD-g-Alg inclusion complexes were investigated. [Chapter 7](#) concludes the previous chapters.