



UNIVERSITÀ DEGLI STUDI DI SALERNO

**Department of Industrial Engineering**

Master's degree in Food Engineering

**Urea adsorption for artificial kidneys:  
synthesis of polyphenylglyoxaldehyde and  
mathematical modeling of its applications**

Thesis in

**Transport Phenomena**

Supervisors:

Prof. Eng. Gaetano Lamberti

Prof. C. F. Van Nostrum

Dr. K.G.F. Gerritsen

Dr. Eng. Diego Caccavo

Dr. Piet Driest

Candidate:

Ciro Scarano  
number 0622800448

**Academic Year 2019/2020**



**Universiteit Utrecht**



**UMC Utrecht**

The synthesis and the characterization of the polymer were performed at the Department of Pharmaceutical Sciences, Faculty of Sciences, Utrecht Universiteit (Utrecht, Netherlands), under the supervision of Prof. C. F. Van Nostrum and dr. Piet Driest while the dynamic experiments were performed at University Medical Center Utrecht under the supervision of dr. K.G.F. Gerritsen during an Erasmus traineeship project.

*Alla mia famiglia*

Questo testo è stato stampato in proprio, in Times New Roman  
La data prevista per la discussione della tesi è il 25/03/21  
Fisciano, 12/03/2021

# Table of contents

<b>Table of contents</b> .....	<b>I</b>
<b>Table of figures</b> .....	<b>V</b>
<b>Table of tables</b> .....	<b>IX</b>
<b>Abstract</b> .....	<b>XI</b>
<b>Abstract (Italian)</b> .....	<b>XIII</b>
<b>Introduction</b> .....	<b>1</b>
1.1 Kidneys and kidneys failure _____	2
1.1.1 Kidneys diseases worldwide	4
1.2 Dialysis _____	5
1.2.1 Peritoneal dialysis	5
1.2.2 Hemodialysis	6
1.2.3 The costs	8
1.3 Wearable artificial kidney (WAK) _____	9
1.3.1 Adsorption of urea	9
1.3.2 Urea adsorbent	10
1.4 State of art _____	11
1.5 Aims of the thesis _____	12
<b>Materials and methods</b> .....	<b>14</b>
2.1 Materials _____	15
2.1.1 Styrene	15
2.1.2 Poly(methacrylic acid) sodium salt solution	15
2.1.3 55% technical grade divinylbenzene (DVB)	16
2.1.4 50% Benzoyl peroxide blend with dicyclohexyl phthalate	16
2.1.5 Aluminum Chloride	17
2.1.6 HBr 48%	17
2.2 Equipment _____	17

2.2.1 Glass reactors	17
2.2.2 Oil bath	18
2.2.3 Laboratory Glassware	18
2.3 Synthesis _____	19
2.3.1 Suspension polymerization	19
2.3.2 Acetylation of polystyrene	22
2.3.3 Kornblum oxidation	24
2.4 Dynamic experiment _____	26
2.5 Analysis _____	28
2.5.1 Infrared spectroscopy	28
2.5.2 Optical microscopy	29
2.5.3 Nitrogen physisorption	29
2.5.4 Analysis on urea binding capacity	30
<b>Modeling .....</b>	<b>32</b>
3.1 Modeling _____	33
3.1.1 Mass balance on the vessel	34
3.1.2 Mass balance of urea in the fluid phase in the adsorption unit	35
3.1.3 Mass balance of urea adsorbed by the polymeric phase	36
3.2 Implementation in COMSOL _____	37
3.2.1 Implementation in COMSOL used for dynamic experiments	37
3.2.2 Implementation in COMSOL used for the single adsorption unit	45
3.2.3 Implementation in COMSOL used for multiple adsorption unit	47
3.2.4 Implementation in COMSOL used for adsorption with generation of urea	50
<b>Results and discussion .....</b>	<b>51</b>
4.1 Synthesis and characterization results _____	52
4.1.1 Infrared spectroscopy results	52
4.1.2. Optical Microscopy results	55
4.1.3. Nitrogen physisorption results	56
4.2.4. Urea analysis results.	56
4.2 Dynamic experiments results _____	57
4.3 Modeling results _____	58
4.3.1 Modeling on the dynamic experiment	58
4.3.2 Simulation of the single adsorption unit	63
4.3.2 Simulation of artificial kidney behavior with continuous generation of urea	66
<b>Conclusions .....</b>	<b>70</b>
5.1 Conclusions _____	71
5.1.1 Introduction	71
5.1.2 Conclusions of the project	71

---

---

**References .....73**





## Table of figures

Figure 1 - Kidney anatomy.....	2
Figure 2 - A case of uremic frost.....	3
Figure 3 - Stages of CKD [2] .....	4
Figure 4 – An example of dialysis.....	5
Figure 5 - A scheme of peritoneal dialysis[3] .....	6
Figure 6 - An example of hemodialysis.....	7
Figure 7 - A scheme of fluctuations between ESKD and normal patients .....	8
Figure 8 - Structural formula of urea.....	9
Figure 9 - A scheme of the pros and cons of the ninhydrin and PGA .....	11
Figure 10 - Roadmap of the artificial kidney development[13] .....	12
Figure 11 - Styrene structure .....	15
Figure 12 - Poly(methacrylic acid) sodium salt structure .....	16
Figure 13 - DVB structure.....	16
Figure 14 - 50% benzoyl peroxide blend with cyclohexyl structure .....	16
Figure 15 - Aluminum Chloride structure .....	17
Figure 16 - A set of glass reactors .....	18
Figure 17 - Oil bath .....	18
Figure 18 - A set of laboratory glassware.....	19
Figure 19 - Scheme of suspension polymerization.....	19
Figure 20 - The glass reactor just before the oil bath .....	21
Figure 21 - Beads of polystyrene during the washing part.....	21
Figure 22 - A sample of polystyrene .....	22
Figure 23 - Acetylation of polystyrene.....	22
Figure 24 - The glass reactor before the heating step .....	23
Figure 25 - Beads during the ice bath.....	23
Figure 26 - Acetylated beads of polystyrene during the washing step .....	24
Figure 27 - A sample of acetylated polystyrene .....	24
Figure 28 - Oxidation of acetylated polystyrene into PGA .....	25
Figure 29 - Beads during oxidation .....	25
Figure 30 - PGA beads during the washing part.....	26
Figure 31 - A sample of PGA beads.....	26
Figure 32 - Glasses columns.....	27
Figure 33 - A glass column filled with beads and PBS .....	27
Figure 34 - A dynamic experiment.....	28
Figure 35 - Perkin Elmer ATRU Spectrum 2 .....	29
Figure 36 - Eclipse TE2000 Microscope.....	29

---

Figure 37 - Micromeritics TriStar 3000.....	30
Figure 38 - A scheme of the dynamic experiment.....	33
Figure 39 - The vessel's balance .....	34
Figure 40 - The balance on the adsorption unit .....	35
Figure 41 - The balance on the polymeric phase .....	36
Figure 42 - An example of set of parameters on COMSOL for a dynamic experiment simulation .....	38
Figure 43 - The Domain Point Probe at the beginning of the adsorption unit .....	39
Figure 44 : The Domain Point Probe at the end of the column in the case of dynamic experiment simulation.....	40
Figure 45 - Implementation of the velocity .....	41
Figure 46 - Equation for Transport Properties 1 .....	41
Figure 47 - Domain for Transport Properties 1 .....	41
Figure 48 - Equation for Concentration 1 .....	42
Figure 49 - Domain of Concentration 1 .....	42
Figure 50 - Equation for Reaction 1 .....	43
Figure 51 - Domain of Reactions 1 .....	43
Figure 52 - Equation for the outflow condition .....	44
Figure 53 - Domain of the outflow condition .....	44
Figure 54 - Equation for the Zero Flux condition.....	45
Figure 55 - Domain of the Zero Flux condition.....	45
Figure 56 - A single adsorption unit.....	46
Figure 57 - The ODE implemented in COMSOL for the single adsorption unit.....	47
Figure 58 - A scheme of a system of cartridges.....	48
Figure 59 - Global equations' section in the case of 3-cartridges system.....	49
Figure 60 - Equation in the "Global Equation 1" section considering the generation term .....	50
Figure 61 - IR spectra of polystyrene, acetylated polystyrene and PGA .....	52
Figure 62 – PGA turning into PGOA .....	53
Figure 63 - All the spectra of PGA samples taken at different times during the extra-oxidation experiment with the machine's software .....	54
Figure 64 - Zoom on the carboxylic acid peak. ....	54
Figure 65 - Beads of polystyrene – 4x magnification.....	55
Figure 66 - Beads of acetylated polystyrene – 4x magnification.....	55
Figure 67 - Beads pf PGA – 4x magnification .....	56
Figure 68 - UBC vs extra ox. Time .....	57
Figure 69 - Experimental data of dynamic experiment.....	58
Figure 70 - Fitting of experimental data, concentration of urea in the vessel against the time .....	59
Figure 71 - Cv vs t with a volumetric flow rate of 60 mL/min .....	60
Figure 72 - Cb vs z with a volumetric flow rate of 60 mL/min .....	60
Figure 73 - Ca vs z with a volumetric flow rate of 60 mL/min .....	61
Figure 74 - Cb vs z with a flow rate of 0.05 mL/min and k calculated with the equation 4.1 .....	62
Figure 75 - Cartridge's length vs Damkohler number.....	63
Figure 76 - Molar flow rate vs t.....	64
Figure 77 - Cv vs t .....	65
Figure 78 - Cv vs t with different cartridges.....	67
Figure 79 - Molar flow rate adsorbed vs t – GEN .....	68

---

---

Figure 80 - Molar flow rate adsorbed vs t - GEN - zoom..... 68



## Table of tables

Table 1 - A comparison between the different urea removal strategy .....	10
Table 2 - Cartridges vs t (90%) .....	66



## Abstract

The thesis was carried out with a joint project, based on the development of an artificial kidney, between the University of Salerno, University of Utrecht and University Medical Center Utrecht. In particular the aim of this thesis was the synthesis and the characterization of a polymer able to adsorb urea and the mathematical modelling of the adsorption process.

The polyphenylglyoxaldehyde (PGA) was the chosen polymer for the study, its synthesis was successfully completed and an urea adsorption capacity of 1.34 mmol/g was produced. After the synthesis different analysis were carried out in order to characterize the polymer. The IR Spectra was performed in order to study and monitor the right oxidation point of the polymer from a quantitative and a quantitatively point of view, the optical microscopy gave important info about the size of the beads of polymer produces, the nitrogen physisorption was performed in order to obtain info about porosity and urea analysis were carried out in order to have info about the efficiency of the adsorbance of the material. The next step was set up some dynamic experiments useful to simulate a dialysis session using the polymer synthesized and obtaining in this way data useful for the modelling part.

The synthesis, the characterization and the dynamic experiments were performed in the Netherlands.

The second part of this thesis, focused on the mathematical model of the adsorption process, led to the use of three equations, 2 partial differential equations to describe the free and the polymer -bounded urea in the adsorber and 1 ordinary differential equation to describe the concentration of the urea in the reservoir (simulating the circulatory system). The model was implemented and solved with the software COMSOL Multiphysics. Most of the model parameters (void grade, initial concentration of urea ecc.) were obtained from the

experiments, while the only fitting parameter was the pseudo kinetic constant  $k$ .

After the determination of the pseudo kinetic constant by fitting the experimental results, simulations were performed with COMSOL considering both the presence of a large amount of urea accumulated in 1 day or a process accounting for the continuum generation of it.

Two “adsorption unit” configurations were considered: the single adsorption unit configuration and the multiple (parallel) adsorption units configuration. Different useful parameters were obtained like the molar flow rate adsorbed by the polymer, the time necessary to adsorb the 90% of urea and the saturation point of the polymer. From the simulations it was found out that the multiple configuration outperform the single adsorption unit configuration. However, increasing above two the number of cartridges (adsorption units) does not improve considerably the adsorption process, therefore the optimum was identified in 2 adsorption units in parallel.

In the future work it would be possible to improve the synthesis working on the homogeneity of the beads and in this way, it could be possible to study from a quantitative point of view the over-oxidation and find the right grade of oxidation to improve the urea binding capacity of the polymer. Furthermore, the modelling could be improved separating the external mass transport and the diffusion inside the polymer pores that in this work were incorporated, along with the reaction rate, in the pseudo kinetic constant.

---



## Abstract (Italian)

Questa tesi è stata portata avanti da un progetto congiunto, basato sullo sviluppo di un rene artificiale, tra l'Università di Salerno, l'Università di Utrecht e l'University Medical Center Utrecht. L'obiettivo della tesi è stata la sintesi e la caratterizzazione di un polimero capace di adsorbire l'urea e la modellazione matematica del processo di adsorbimento.

Il polifenilgliossaldeide (PGA) è stato il polimero scelto per questo lavoro di tesi, la sua sintesi è stata completata con successo e un polimero con una capacità di adsorbire urea di 1.34 mmol/g è stato sintetizzato. Dopo la sintesi diverse analisi sono state portate a termine per caratterizzare il polimero. Lo spettro a infrarossi è stato fatto per studiare e monitorare il giusto punto di ossidazione del polimero da un punto di vista qualitativo e quantitativo, la microscopia ottica ha dato importanti informazioni sulla porosità e analisi sull'urea sono state fatte per avere informazioni sull'efficienza di adsorbimento del materiale. Lo step successivo è stato fare degli esperimenti dinamici utili per simulare una sessione di dialisi usando il polimero sintetizzato e ottenendo così dati utili per la parte modellistica.

La sintesi, la caratterizzazione e gli esperimenti dinamici sono stati fatti in Olanda.

La seconda parte della tesi, focalizzata sul modello matematico del processo di adsorbimento, ha portato all'uso di tre equazioni, 2 equazioni differenziali alle derivate parziali e una 1 equazione differenziale ordinaria per descrivere la concentrazione di urea in un vessel (che simula il sistema circolatorio). Il modello è stato implementato e risolto con il software COMSOL Multiphysics. La maggior parte dei parametri del modello (il grado di vuoto, la concentrazione iniziale di urea ecc.) sono stati ottenuti dagli esperimenti, mentre l'unico parametro di fitting è stato la costante pseudo cinetica.

Dopo la determinazione della costante pseudo cinetica con il fitting dei risultati sperimentali, le simulazioni sono state fatte con COMSOL considerando sia la presenza di una grande quantità di urea

---

accumulata in 1 giorno sia un processo che prende in considerazione la continua generazione della stessa.

Due configurazioni delle “unità di adsorbimento” sono state considerate: la singola unità di adsorbimento e la configurazione multipla (in parallelo). Diversi parametri utili sono stati ottenuti come il flusso molare di urea adsorbita dal polimero, il tempo necessario per adsorbire il 90% di urea e il punto di saturazione del polimero. Dalle simulazioni è risultato che la configurazione multipla supera di gran lunga la configurazione di adsorbimento singola. Tuttavia, aumentando oltre due il numero di cartucce (unità di adsorbimento) il processo di adsorbimento non migliora ulteriormente, perciò l’ottimo è stato identificato in 2 unità di adsorbimento in parallelo.

In future potrebbe essere possibile migliorare la sintesi lavorando sull’omogeneità delle sfere e così potrebbe essere possibile studiare da un punto di vista quantitativo la sovraossidazione e trovare il giusto grado di ossidazione per migliorare la capacità di legarsi all’urea del polimero. Inoltre, la modellazione potrebbe essere migliorata separando il trasporto di massa esterno e la diffusione nei pori del polimero che in questo lavoro sono stati inclusi, insieme alla velocità di reazione, nella costante pseudocinetica.

---

## References

1. Jong, J.A.W., *Bottom-up Development of Urea Sorbents for Dialysate Regeneration*. 2019, Utrecht University.
2. *Global Facts: About Kidney Disease*. Available from: <https://www.kidney.org/kidneydisease/global-facts-about-kidney-disease>.
3. Disease, N.I.o.D.a.D.a.K. *Peritoneal Dialysis*. Available from: <https://www.niddk.nih.gov/health-information/kidney-disease/kidney-failure/peritoneal-dialysis>.
4. Mushi, L., P. Marschall, and S. Fleßa, *The cost of dialysis in low and middle-income countries: a systematic review*. BMC Health Serv Res, 2015. **15**: p. 506.
5. Saran, R., et al., *US Renal Data System 2018 Annual Data Report: Epidemiology of Kidney Disease in the United States*. Am J Kidney Dis, 2019. **73**(3 Suppl 1): p. A7-A8.
6. Cicchetti, A.a.R., Matteo and Codella, Paola and Ridolfi, Alessandro, *I costi socio-sanitari dell'insufficienza renale cronica*. Farmacoeconomia e percorsi terapeutici, 2011. **12**: p. 21--8.
7. Culleton, B.F., et al., *Effect of frequent nocturnal hemodialysis vs conventional hemodialysis on left ventricular mass and quality of life: a randomized controlled trial*. JAMA, 2007. **298**(11): p. 1291-9.
8. Chertow, G.M., et al., *In-center hemodialysis six times per week versus three times per week*. N Engl J Med, 2010. **363**(24): p. 2287-300.
9. Weiner, I.D., W.E. Mitch, and J.M. Sands, *Urea and Ammonia Metabolism and the Control of Renal Nitrogen Excretion*. Clin J Am Soc Nephrol, 2015. **10**(8): p. 1444-58.

10. Shinaberger, C.S., et al., *Longitudinal associations between dietary protein intake and survival in hemodialysis patients*. Am J Kidney Dis, 2006. **48**(1): p. 37-49.
  11. Singh, L.R., T.A. Dar, and F. Ahmad, *Living with urea stress*. J Biosci, 2009. **34**(2): p. 321-31.
  12. Vanholder, R.a.G., Tessa and Glorieux, Griet, *Urea and chronic kidney disease: the comeback of the century?(in uraemia research)*. Nephrology Dialysis Transplantation, 2018. **33**(1): p. 4--12.
  13. van Gelder, M.K., et al., *From portable dialysis to a bioengineered kidney*. Expert Rev Med Devices, 2018. **15**(5): p. 323-336.
  14. Fogler, S., *Elements of Chemical Reaction Engineering*. 4th ed. ed. 2006.
-



