

**DESIGN AND SYNTHESIS OF MULTIFUNCTIONAL CHITOSAN FROM  
WATER-BASED REACTION SYSTEM FOR POTENTIALLY  
BIOMEDICAL MATERIALS**

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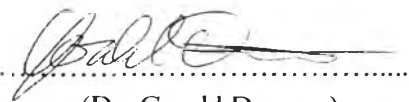
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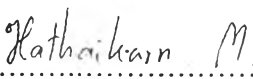
  
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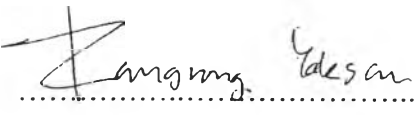
  
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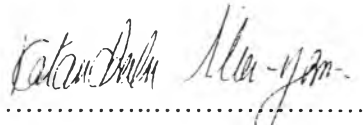
  
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## ABSTRACT

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The present work focuses on molecular design, synthesis, systematic studying of multifunctional chitosan to use as promising biomedical materials. Here, the strategies of nanoparticle self assembly and hybridization of chitosan-inorganic nanoparticle are proposed to produce multifunctional chitosan. However, the use of chitosan without acidic solvent is still required. Thus, the multifunctional chitosan from 2 strategies are prepared by chemical functionalization based on water-based reaction system and mild condition. In the first part, biomolecules, phenylalanine and polyethylene glycol, are derivatized on chitosan chain via CS-HOBt water soluble system and conjugating reaction. This chitosan derivative shows the colloidal stability in water, nanoparticle forming, and ability to form allergen. This design system is proposed to use in allergen delivery system. In the second part, chitosan is functionalized with active molecule called as oxanorbornadiene. The chitosan-oxanorbornadiene is proposed as a novel type of chitosan derivative which can be further coupled with azido-modified substrates to provide various types of functional groups on chitosan chain via Cu-free Click. The reaction can be done in aqueous solution without catalyst and purification steps. In the final part, chitosan-oxanorbornadiene is developed to be a water-soluble chitosan derivative to hybridize with inorganic nanoparticles, azido-gold nanoparticles. The success of hybridization provides the gold aggregation via Cu-free Click. This part is extended to use this chitosan-oxanorbornadiene as a linker between gold nanoparticles and antigens to provide the gold aggregated acceleration in naked-eye detection of antigens.

## บทคัดย่อ

เจตสุดา จิรวุฒิวงศ์ชัย : การออกแบบและสังเคราะห์ไคโตซานหลากหลายฟังก์ชันจากระบบปฏิกิริยาพื้นฐานในน้ำ เพื่อความเป็นไปได้สำหรับวัสดุทางชีวแพทย์ (Design and Synthesis of Multifunctional Chitosan from Water-based Reaction System for Potentially Biomedical Materials) อ. ที่ปรึกษา: ศาสตราจารย์ ดร. สุวบุญ จิรชาญชัย 158 หน้า

วิทยานิพนธ์ฉบับนี้มุ่งเน้นถึงการออกแบบโมเลกุล การสังเคราะห์ และการศึกษาอย่างมีระบบของไคโตซานหลากหลายฟังก์ชัน เพื่อใช้เป็นวัสดุทางชีวแพทย์อย่างเป็นไปได้ ในงานนี้ ผู้วิจัยเลือกกลวิธี การรวมแบบอัดโนมัติ และการผสมระหว่างไคโตซานและอนุภาคอนินทรีย์ระดับนาโน เพื่อการผลิตไคโตซานหลากหลายฟังก์ชัน อย่างไรก็ตามการหลีกเลี่ยงการใช้สารละลายไคโตซานในอะซิติกยังคงมีความต้องการ ดังนั้น ไคโตซานหลากหลายฟังก์ชันจากกลวิธี 2 แบบข้างต้น จึงถูกเตรียมโดยการเติมแต่งหมู่ฟังก์ชันทางเคมีบนพื้นฐานของระบบปฏิกิริยาพื้นฐานในน้ำ และปฏิกิริยาที่ไม่รุนแรง ในส่วนแรก โมเลกุลทางชีวภาพ ได้แก่ ฟินิลอะลาไมน และพอลิเอทิลีนไกลคอล ถูกเติมแต่งบนสายโซ่ไคโตซานผ่านระบบ CS-HOBt ที่ละลายน้ำและผ่านปฏิกิริยาแบบจับคู่ อนุพันธ์ไคโตซานนี้แสดงสมบัติคอลลอยด์ได้ในน้ำ มีขนาดอนุภาคระดับนาโน และมีความสามารถในการกักเก็บสารก่อภูมิแพ้ (allergen) ระบบที่ถูกออกแบบนี้ถูกเสนอขึ้นเพื่อใช้ในระบบขนส่งสารก่อภูมิแพ้ ในส่วนที่สอง ไคโตซานถูกเติมแต่งฟังก์ชันด้วยโมเลกุลที่มีความสามารถในการกระตุ้น ที่เรียกว่า ออกซานอร์บอร์นะไดอิน (oxanorbomadiene) ไคโตซาน-ออกซานอร์บอร์นะไดอินนี้ถูกเสนอให้เป็นอนุพันธ์ไคโตซานแบบใหม่ที่สามารถเข้าคู่กันกับ อะซิโดโมดิฟายด์ซัพสเตรคหลายๆ แบบ เพื่อก่อให้เกิดหมู่ฟังก์ชันหลากหลายแบบบนสายโซ่ไคโตซานผ่านทางปฏิกิริยาเคมีคลิกแบบปราศจากคอปเปอร์ ปฏิกิริยานี้สามารถถูกเตรียมได้ในสารละลายที่มีน้ำเป็นองค์ประกอบโดยปราศจากสารเร่งปฏิกิริยา (catalyst) และกระบวนการทำสารให้บริสุทธิ์ ในส่วนสุดท้าย ไคโตซาน-ออกซานอร์บอร์นะไดอินถูกพัฒนาให้เป็นอนุพันธ์ไคโตซานที่ละลายน้ำได้ เพื่อผสมกับอนุภาคอนินทรีย์ระดับนาโน ที่เรียกว่า อนุภาคอะซิโด-ทอง ความสำเร็จของการผสมก่อให้เกิดการรวมกลุ่มของอนุภาคทองผ่านทางปฏิกิริยาเคมีคลิกแบบปราศจากคอปเปอร์ ในงานส่วนนี้ถูกขยายให้ใช้ไคโตซาน-ออกซานอร์บอร์นะไดอินเป็นตัวเชื่อมระหว่างอนุภาคทองระดับนาโนและแอนติเจนเพื่อทำให้เกิดการเร่งการรวมกลุ่มของอนุภาคทองระดับนาโนสำหรับการตรวจสอบสารแอนติเจนด้วยตาเปล่า

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