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 OF DEXTRIN-ZIDOVUDINE CONJUGATE
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 คอนจูเกต (SYNTHESIS, *IN VITRO* AND *IN VIVO* STUDIES OF DEXTRIN-
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ซีโดวูดินเป็นยารักษาโรคเอดส์ซึ่งเกิดจากเชื้อเอชไอวี โดยรักษาเดี่ยวหรือร่วมกับยาต้าน
 ไวรัสชนิดอื่น เนื่องด้วยค่าครึ่งชีวิตของซีโดวูดินสั้นดังนั้นจึงต้องให้ยาในขนาดสูงและบ่อยครั้งใน
 การรักษาการติดเชื้อเอชไอวีซึ่งมีผลเสียต่อความเป็นพิษของยาสูง เพื่อที่จะแก้ข้อเสียเหล่านี้ จึงได้
 สังเคราะห์เด็กชดริน-ซีโดวูดินคอนจูเกตขึ้นเพื่อให้เวลาในการปลดปล่อยยาซีโดวูดินนานขึ้น ขั้น
 แรกในการสังเคราะห์ ซีโดวูดินทำปฏิกิริยากับซัคซินิกแอนไฮไดรด์ ได้ซัคซินิเลทเทตซีโดวูดิน
 จากนั้นคอนจูเกตกับเด็กชดริน ตรวจสอบคุณลักษณะโครงสร้างของเด็กชดริน-ซีโดวูดินคอนจูเกต
 โดยวิธีอินฟราเรดและโปรตอนนิวเคลียร์แมกเนติก เด็กชดริน-ซีโดวูดินคอนจูเกตบรรจุยาได้ 18.92
 เปอร์เซ็นต์ ตรวจสอบการปลดปล่อยของซีโดวูดินอิสระและซัคซินิเลทเทตซีโดวูดินจากเด็กชดริน-
 ซีโดวูดินคอนจูเกตนอกร่างในสารละลายบัฟเฟอร์ที่พีเอช 5.5, 7.4 และในพลาสมาของมนุษย์
 ซีโดวูดินและซัคซินิเลทเทตซีโดวูดินรวมปลดปล่อยจากคอนจูเกต 1.4 % ที่พีเอช 5.5, 41.7 % ที่พี
 เอช 7.4 และ 78.4 % ในพลาสมาของมนุษย์หลังจาก 24 ชั่วโมง การปลดปล่อยยาสมบูรณ์ใน
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 เม็ดเลือดแดง พบว่ามีผลต่อการสลายเม็ดเลือดแดงต่ำ การศึกษาความเป็นพิษต่อเซลล์ของเด็กช
 ดริน-ซีโดวูดินคอนจูเกตในเซลล์เยื่อของปอด พบว่าคอนจูเกตแสดงความเป็นพิษต่ำกว่าซีโดวูดิน
 อิสระ การศึกษาการปลดปล่อยยาในกายได้ทดสอบในหนูโดยการให้เด็กชดริน-ซีโดวูดินคอนจูเกต
 และซีโดวูดินอิสระโดยการฉีดเข้าทางหลอดเลือดดำ เด็กชดริน-ซีโดวูดินคอนจูเกตแสดงการ
 ปลดปล่อยยาซีโดวูดินเนิ่นนานในกระแสเลือดเมื่อเปรียบเทียบกับซีโดวูดินอิสระ คุณสมบัติทาง
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ลายมือชื่อนิสิต.....ศุมาลี วรรณชาชัยสิทธิ์.....
 ลายมือชื่ออาจารย์ที่ปรึกษา.....อุบลทิพย์ นิมมานนิตย์.....

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SUMALEE WANNACHAIYASIT: SYNTHESIS, *IN VITRO* AND *IN VIVO* STUDIES OF DEXTRIN-ZIDOVUDINE CONJUGATE. THESIS ADVISOR: ASSOC. PROF. UBONTHIP NIMMANNIT, Ph. D. THESIS COADVISOR: PROF. RUTH DUNCAN, Ph. D. 146 pp.

Zidovudine was used for the treatment of acquired immunodeficiency syndrome (AIDS) caused by human immunodeficiency viruses (HIV) as a single or combination therapies. The short plasma half-life of zidovudine demands a frequent and large dose regimen for the treatment of HIV infections resulting in a high risk of toxicities. To overcome these drawbacks dextrin-zidovudine conjugate was synthesized to prolong the release of zidovudine. Zidovudine firstly reacted with succinic anhydride and the succinylated zidovudine was subsequently conjugated with dextrin. The structure of the dextrin-zidovudine conjugate was characterized by FT-IR and ¹H-NMR spectroscopy. The drug loading in the dextrin-zidovudine conjugate was 18.92 percent. The *in vitro* releases of free zidovudine and succinylated zidovudine from the dextrin-zidovudine conjugate were investigated in buffer solutions at pH 5.5, 7.4 and in human plasma. The total released zidovudine and succinylated zidovudine from the conjugate were 1.4 % at pH 5.5, 41.7 % at pH 7.4 and 78.4 % in human plasma after 24 h. The drug release was complete in human plasma within 48 h. The study of red blood cell lysis showed that the dextrin-zidovudine conjugate exhibited low hemolytic effect. The cytotoxicity of the dextrin-zidovudine conjugate was investigated in lung epithelial cells and the result showed that the dextrin-zidovudine conjugate was less toxic than free drug. An *in vivo* drug release study was conducted in rats. The dextrin-zidovudine conjugate and free zidovudine were administered by intravenous route. The dextrin-zidovudine conjugate showed prolonged release of zidovudine compared with free zidovudine in blood circulation. The pharmacokinetic properties of the dextrin-zidovudine conjugate such as plasma half-life were improved. The zidovudine plasma half-life of the dextrin-zidovudine conjugate was extended from 1.3 h to 19.3 h.

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