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นายจตุพล เจริญกิจไพบูลย์

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จุฬาลงกรณ์มหาวิทยาลัย

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DEVELOPMENT OF DRY POWDER COATING TECHNIQUE FOR PELLETS

Mr. Chatuphon Charoenkitpaiboon



ศูนย์วิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

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การเคลือบในรูปแบบผงแห้งเป็นวิธีการเคลือบวิธีใหม่โดยใช้เพียงพอลิเมอร์ในรูปแบบผงแห้งเท่านั้นและไม่มีการใช้ของเหลวใดๆ ตลอดกระบวนการผลิต วัตถุประสงค์ในการวิจัยนี้คือ เพื่อศึกษาความเป็นไปได้ในกระบวนการเคลือบในรูปแบบผงแห้งอย่างแท้จริงและศึกษาปัจจัยที่มีอิทธิพลต่อการเกาะติดของพอลิเมอร์บนสารแกน(เพลเลท) ปัจจัยที่ทำการศึกษาได้แก่ อัตราการใช้พอลิเมอร์ ปริมาณพอลิเมอร์ทั้งหมด ขนาดของเพลเลท ขนาดของพอลิเมอร์ ความขรุขระและความชื้นของพื้นผิวเพลเลทตั้งต้น และความเป็นไปได้ในการเคลือบเพลเลทชั้นที่สอง

โพรพาราโนลอลไฮโดรคลอไรด์เพลเลทตั้งต้นเตรียมได้โดย วิธีเอกซ์ทรูชัน-สเฟียโรในเซชัน และนำมาเคลือบด้วยพอลิเมอร์ออยดรากิต อี (Eudragit® E) ในรูปแบบผงแห้งเมื่อใช้วิธีการเคลือบรูปแบบผงแห้งโดยการใช้หม้อเคลือบธรรมดา ออยดรากิต อี นั้นมีค่าอุณหภูมิแปรผ่านแก้ว (Tg) ต่ำ (45-50 องศาเซลเซียส) และมีคุณสมบัติการเกาะติดที่ดี มีการศึกษาถึงคุณสมบัติทางกายภาพและคุณสมบัติในการปลดปล่อยตัวจากเพลเลทตั้งต้น และเพลเลทที่ถูกเคลือบแล้ว จากการทดลองพบว่า การใช้พอลิเมอร์ในปริมาณที่สูงขึ้นสามารถทำให้พื้นผิวที่เคลือบเรียบขึ้น และเมื่อมีการควบคุมขนาดของเพลเลทให้คงที่ พอลิเมอร์ในรูปแบบผงแห้งที่ใช้เคลือบที่มีขนาดเล็กกว่า จะให้ผลการเกาะติดการกระจายความร้อนที่ดี และการกระจายตัวของฟิล์มที่สม่ำเสมอกว่าพอลิเมอร์ขนาดใหญ่ และยังพบว่า เพลเลทตั้งต้นที่มีผิวขรุขระมากขึ้นจะทำให้ประสิทธิภาพในการเคลือบสูงขึ้น และในเพลเลทตั้งต้นที่มีความชื้นสูงอาจจะเป็นผลให้การเกาะติดของพอลิเมอร์ดีขึ้นได้ สำหรับการเคลือบเพลเลทชั้นที่สองนั้นให้ผลดีในการเพิ่มความหนาของชั้นฟิล์มแต่ทำให้เกิดลักษณะที่ไม่พึงประสงค์ในการเกาะติดกันของเพลเลทซึ่งเป็นผลมาจากความร้อนที่มีผลต่อการอ่อนนุ่มของพอลิเมอร์ที่เคลือบในชั้นแรก มีการศึกษาการเปลี่ยนแปลงทางด้านเคมีของแข็งของเพลเลทตั้งต้นและเพลเลทที่เคลือบแล้ว โดยวิธีฟูเรียร์แทรนสฟอร์มอินฟราเรดสเปกโตรสโคปี (FTIR) เอกซ์เรย์ดิฟแฟรคโทรมเมทรี (XRPD) และดิฟเฟอเรนเชียลสแกนนิ่งแคลอริเมทรี (DSC) ไม่พบการเปลี่ยนแปลงทางด้านเคมีของแข็งของทุกองค์ประกอบ และไม่เกิดความไม่เข้ากันระหว่างตัวยาและพอลิเมอร์หรือสารช่วยอื่นในสูตรตำรับ ดังนั้นเทคนิคการเคลือบในรูปแบบผงแห้งนี้จึงอาจเป็นทางเลือกหนึ่งในการเคลือบสารแกนในอนาคต โดยไม่มีการใช้น้ำหรือสารละลายอินทรีย์ที่เป็นอันตรายต่อสิ่งแวดล้อมเลย

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ลายมือชื่อผู้ผลิต..... จุฑพล เจริญกิจไพบูลย์
ลายมือชื่ออาจารย์ที่ปรึกษา.....
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/POLYMER

CHATUPHON CHAROENKITPAIBOON: DEVELOPMENT OF DRY POWDER
COATING TECHNIQUE FOR PELLETS. THESIS ADVISOR: NARUEPORN
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POJ KULVANICH, Ph.D. ,270 pp. ISBN 974-17-5363-2.

Dry powder coating is an innovative coating method utilizing only dry polymer powder without applying any liquid throughout the process. Objectives of this work were to study the feasibility of this dry powder coating technique and to investigate the parameters that affect polymer adhesion on core material (pellets). The parameters studied were polymer application rate, loading amount of polymer, pellet size, polymer size, surface roughness and moisture content of core pellets and the possibility of secondary layer coating.

Propranolol hydrochloride core pellets were prepared by extrusion-spheronization technique and were coated with Eudragit[®] E polymer powder using the powder coating technique in a conventional coating pan. Eudragit[®] E polymer powder had low glass transition temperature (45-50 °C) and good adhesion property. Physical characteristics and drug release characteristics of core and coated pellets were investigated. It was found that higher polymer loading could improve the smoothness of the coating surface. At a constant pellet size, smaller polymer particle size was proven to promote better adhesion, better heat dissipation and more uniform film distribution than larger particles. The results also showed that the more surface roughness the core pellets exhibited, the higher coating efficiency was observed. And higher moisture content on surface of core pellets might result in better polymer adhesion. It was possible to apply the secondary coating layer with an appreciable increase in film thickness. However, the process induced undesirable pellet aggregation due to thermosoftening of the primary coating material. The solid state characterization of core and coated pellets was also investigated by Fourier transform infrared spectroscopy (FTIR), x-ray powder diffractometry (XRPD) and differential scanning calorimetry (DSC). Solid state characteristics of every component remained unchanged. Also, the results indicated that incompatibility between the drug and polymer or other excipients in the formulation did not take place. Thus, with a minor process adjustment, this dry powder coating technique may be considered as an alternative method in the future for coating core materials without the use of water or environmentally hazardous organic solvents involved.

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List of Abbreviation

| | |
|-------------------|--|
| DSC | differential scanning calorimetry |
| $^{\circ}2\theta$ | degree 2 theta |
| $^{\circ}C$ | degree Celsius (centigrade) |
| cm | centimeter (s) |
| cm^{-1} | per centimeter (s) |
| CV | coefficient of vriation |
| et al. | et alli, and others |
| gm | gram (s) |
| HCl | hydrochloric acid |
| hr | hour (s) |
| FTIR | fourier transform infrared |
| <i>k</i> | coefficient constant or rate constant |
| m^2/gm | square meter per gram |
| MCC | microcrystalline cellulose (Avicel [®] PH 101) |
| mg | milligram (s) |
| min | minute (s) |
| ml | milliliter (s) |
| mm | millimeter (s) |
| mm^2 | squared millimeter (s) |
| nm | nanometer (s) |
| No. | number |
| % | percent |
| pH | the negative logarithm of the hydrogen ion concentration |
| q.s. | make to volume |
| r^2 | coefficient of determination |
| RH | relative humidity |
| rpm | revolution per minute |
| SD | standard deviation |
| SEM | scanning electron microscopy |
| Tg | glass transition temperature |
| UV-VIS | ultraviolet-visible |

| | |
|-----------|--------------------------|
| V/V | volume by volume |
| W/V | weight by volume |
| W/W | weight by weight |
| XRPD | x-ray powder diffraction |
| λ | wavelength |



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