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DEVELOPMENT OF THIN FILMS AS TABLET DEGRADATION INDICATOR

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คู่มือ นิตยวรรณะ : การพัฒนาฟิล์มบางเพื่อใช้เป็นตัวชี้วัดการเสื่อมสลายของยาเม็ด
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วัตถุประสงค์การศึกษา เพื่อพัฒนาสูตรคาร์บฟิล์มบางเพื่อเป็นตัวชี้วัดการเสื่อมสลายโดยเคลือบคิดที่ผิวเม็ดยา ในการศึกษาเตรียมฟิล์มเป็น 3 ชั้น ฟิล์มในแต่ละชั้นใช้ไฮดรอกซีโพรพิลเมธิลเซลลูโลสเป็นสารก่อก่อฟิล์ม ฟิล์มชั้นแรกประกอบด้วยสารสกัดจากกะหล่ำปลีสีม่วงซึ่งมีคุณสมบัติเป็นตัวชี้วัดการเปลี่ยนแปลงความเป็นกรด-เบส ฟิล์มชั้นกลางมีส่วนผสมของพอลิเมอร์พอลิเอินไอโซโพรพิลอะคริเลอไมด์ (poly-N-isopropylacrylamide) ซึ่งทำหน้าที่เป็นชั้นกีดขวางที่ขึ้นต่อการเปลี่ยนแปลงของอุณหภูมิ ฟิล์มชั้นสุดท้ายเป็นฟิล์มเบส เมื่อนำฟิล์มบางที่เตรียมไปทำการทดสอบที่สภาวะอุณหภูมิ 60 องศาเซลเซียสและความชื้นสัมพัทธ์ 20 เปอร์เซ็นต์ พบว่าการหดตัวของพอลิเมอร์พอลิเอินไอโซโพรพิลอะคริเลอไมด์ เมื่อได้รับอุณหภูมิสูงมีผลต่ออัตราการปลดปล่อยของสารสกัดจากกะหล่ำปลีสีม่วงผ่านฟิล์มชั้นกลาง และทำการเปรียบเทียบการอัตราการเปลี่ยนแปลงสีของฟิล์มแต่ละสูตรคาร์บ โดยสร้างกราฟความสัมพันธ์ระหว่างค่าปริมาณสีแดง (a^* value) กับเวลา โดยใช้การประเมินทางสถิติโดยการวิเคราะห์ความแปรปรวนของค่าเฉลี่ยพื้นที่ได้กราฟของฟิล์มแต่ละสูตรคาร์บ และโดยการเปรียบเทียบค่าความแตกต่าง (f_1) และความเหมือน (f_2) ของลักษณะการเปลี่ยนแปลงสีในช่วงเวลาจนถึงจุดสิ้นสุด การศึกษานี้ต้องการพัฒนาสูตรฟิล์มบางเพื่อเป็นตัวชี้วัดการเสื่อมสลายของตัวยาชนิดแบบ 2 ชนิด คือ กลัยเบนคลาไมด์และแอสไพริน ได้ทำการหาคุณลักษณะการเปลี่ยนแปลงโครงสร้างผลึกของกลัยเบนคลาไมด์ที่มีผลต่อค่าการละลายของตัวยา และมีการวิเคราะห์หาปริมาณสารสลายตัว (กรดซาลิไซลิก) ของแอสไพริน พบว่ากลัยเบนคลาไมด์มีค่าการละลายที่ลดลงต่ำกว่า 0.06 มิลลิกรัมต่อมิลลิตร เมื่อเก็บที่สภาวะอุณหภูมิ 60 องศาเซลเซียสและความชื้นสัมพัทธ์ 20 เปอร์เซ็นต์ ระยะเวลา 14 วัน ขณะที่ยาเม็ดแอสไพรินพบปริมาณสารสลายตัวเกินปริมาณที่กำหนด 0.3 เปอร์เซ็นต์ โดยน้ำหนักเมื่อเก็บที่สภาวะอุณหภูมิ 60 องศาเซลเซียสและความชื้นสัมพัทธ์ 75 เปอร์เซ็นต์ในระยะเวลา 18 วัน การมองเห็นการเปลี่ยนแปลงสีด้วยตาเปล่าเกิดขึ้นในระยะเวลาที่สอดคล้องกับการเปลี่ยนแปลงของตัวยาคำคัญในผลิตภัณฑ์ยาเม็ดกลัยเบนคลาไมด์และยาเม็ดแอสไพริน ผลการทดลองนี้ชี้ให้เห็นว่าระบบฟิล์มบางนี้สามารถนำไปพัฒนาให้เหมาะสมสำหรับชี้วัดการเสื่อมสลายของตัวยาคำคัญอื่นๆ ที่มีอุณหภูมิเป็นปัจจัยการเสื่อมสลายหลักสำหรับยาเม็ดได้

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4776565633 : MAJOR MANUFACTURING PHARMACY

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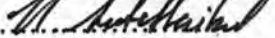
The experiment aimed to design thin film as drug degradation indicator to be placed on the surface of tablets. The approach was to prepare thin films in three layers by using hydroxypropyl methylcellulose as film base. The first layer contained red cabbage extract as a source of pH indicator (anthocyanin). The middle layer contained poly-N-isopropylacrylamide (PNIAAm) acting as thermo sensitive polymeric barrier. The last layer was alkaline layer. The thin film was produced and evaluated at 60°C, 20%RH as a function of time. The result showed that the contraction of PNIAAm after exposure to high temperature effects the release rate of red cabbage extract through thin film. The plot between red color parameter, a* value and time was used to compare the difference of each thin film formulation. ANOVA and Model Independent Methods (difference factor (f_1) and similarity factor (f_2)) were used to evaluate the profiles of a*value before reaching the end point. Thin films were further formulated and used as tablet degradation detector of two model drugs, glibenclamide and aspirin. Glibenclamide was characterized for solid state transformation and its effect on solubility. Aspirin was evaluated for the rate of chemical degradation to salicylic acid. The solubility of amorphous glibenclamide was decreased below 0.06 mg/ml after storage at 60°C, 20%RH for 14 days. While aspirin commercial tablets increased the degradation product (salicylic acid) reaching the limit of 0.3% by weight at 60 °C, 75%RH after 18 days. The color change in thin film correlated well with the degradation rate of glibenclamide and aspirin tablets and was able to visually observe the change. The results indicated that this indicator system can be tailor-made to produce thin film suited for other drugs in detecting degradation which is due mainly to temperature.

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ABBREVIATIONS

| | | |
|--------------------|---|---|
| A | = | aspirin |
| A_0 | = | the initial amount of aspirin in the experiment |
| A_{dgrd} | = | the mass of aspirin degraded |
| A_{rem} | = | the mass of aspirin remaining |
| $^{\circ}\text{C}$ | = | degree Celsius |
| cm | = | centimeter |
| cm^2 | = | centimeter squared |
| CTIs | = | critical temperature indicators |
| CTTIs | = | critical temperature/time integrators |
| DF | = | dilution factor |
| DSC | = | differential scanning calorimetry |
| et al. | = | <i>et alii</i> , 'and others' |
| f_1 | = | difference factor |
| f_2 | = | similarity factor |
| FDA | = | Food and Drug Administration |
| g | = | gram |
| GB | = | glibenclamide |
| HPLC | = | high performance liquid chromatography |
| HPMC | = | hydroxylpropyl methylcellulose |
| K_{app} | = | apparent rate constant |
| l | = | liter |
| LCST | = | lower critical solution temperature |
| LN | = | log normal |
| mg | = | milligram(s) |
| min | = | minute(s) |
| ml | = | milliliter(s) |
| mol/l, M | = | mole per liter |
| mm | = | millimeter |
| N | = | normal (concentration) |
| nm | = | nanometer |

| | | |
|------------|---|--|
| pH | = | the negative logarithm of the hydrogen concentration |
| PNIAAm | = | poly-N-isopropylacrylamide |
| psi | = | pound per square inch |
| RH | = | relative humidity |
| RSD | = | relative standard deviation |
| Rt | = | cumulative percentage dissolved of Reference product at time t |
| SA | = | salicylic acid |
| S.D. | = | standard deviation |
| sec | = | second(s) |
| Tt | = | cumulative percentage dissolved of Test product at time t |
| TTIs | = | time-temperature Integrators or Indicators |
| μ l | = | microliter(s) |
| μ g | = | microgram(s) |
| V | = | volume |
| v/v | = | volume by volume |
| w/v | = | weight by volume |
| w/w | = | weight by weight |
| XRPD | = | x-ray powder diffractometry |
| % | = | percentage |
| Δ H | = | enthalpies |