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CHARACTERISATION AND EVALUATION OF PREGELATINISED SAGO STARCH AS DIRECT COMPRESSION MATERIALS

Field of Study: Pharmaceutical Technology

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ABSTRACT

This study aimed to produce new directly compressible materials from a local sago starch. The sago starch was pregelatinised at 65°C with four different heating times followed by oven drying. The pregelatinised sago starches (PS) were evaluated as directly compressible materials including their properties at molecular, particle and powder level in addition to their functional properties in directly compressible Paracetamol tablet formulations. Analysis of FT-IR and ^{13}CNMR spectra revealed that pregelatinisation did not alter the chemical structure of sago starch. XR-D patterns of sago starch showed characteristics of C-type while PS exhibited A-type, as the degree of crystallinity decreased with increasing heating time. DSC curves showed pregelatinisation increased gelatinisation temperature (T_o), peak temperature (T_p), and degree of gelatinisation (DG), narrowed gelatinisation temperature range ($T_c - T_o$) and decreased the melting enthalpy (ΔH) of sago starch, becoming more pronounced with increased heating time. SEM observations showed more sago starch granules lost their surface smoothness and more irregular shapes appeared as the heating time increased. PS showed higher swelling power (SP) at ≤ 55˚C and water solubility index (WSI) at ≤ 65˚C than sago starch. Longer heating time produced PS with lower amylosa content, higher viscosity, SP and WSI. Powder flow evaluations and powder compacts analysis by Heckel and Kawakita equations, mechanical properties and lubricant sensitivity revealed pregelatinisation improved flowability, compressibility, compactibility and lubricant sensitivity of sago starch, with the order PS4>PS3>PS2>PS1>sago starch. PS4 flowability, compressibility and compactibility was comparable to Spress® B820 but showed lower lubricant sensitivity. Compared to Avicel PH 101, PS4 flowability was superior but its compressibility, compactibility and lubricant sensitivity were inferior. Based on the findings, PS4 was the best candidate for directly compressible excipient

among PS. Evaluation on the loading capacities for Avicel PH 101, PS4 and Spress® B820 relative to poorly compressible Paracetamol reached up to 70.16%, 60.97% and 59.16% W/W respectively. Paracetamol tablets formulated with Avicel PH 101 (Formulation 1) showed the fastest disintegration times, followed by those formulated with PS4 (Formulation 3) and Spress® B820 (Formulation 2) with disintegration times less than 2 minutes, indicating good disintegration properties. However, Formulation 1 did not release 80% of Paracetamol within 30 minutes as required by the USP 27. Dissolution profiles of Formulation 2 and Formulation 3 were similar, releasing > 80% of Paracetamol within 20 minutes and completely releasing of Paracetamol within 25 minutes. Introducing Avicel PH 101 and Sodium starch glycolate in Formulation 2 and Formulation 3, hence identified as Formulation 4 and 5 respectively, showed significantly shortened disintegration times and released > 80% of Paracetamol within 5 minutes. Formulation 4 and Formulation 5 released 100% and 99.95% of Paracetamol respectively within 15 minutes. Their dissolution efficiencies differ by 0.19%, indicating similar dissolution profiles and bio-equivalency. Results of accelerated stability study at conditions of 40°C ± 2°C / 75% RH ± 5% RH for 3 months and 6 months storage showed Formulations 4 and 5 were stable. As a conclusion, this study found that PS4 has the potential as a directly compressible excipient and its characteristics and performances were comparable to Spress® B820.

ABSTRAK

Tujuan kajian ini adalah untuk menghasilkan bahan baru cetak terus daripada kanji sagu tempatan. Kanji sagu dipragelatinasikan pada suhu 65ºC dengan menggunakan empat masa pemanasan berlainan diikuti dengan pengeringan dalam ketuhar. Kanji sagu yang telah dipragelatinasi (PS) dinilai sebagai bahan cetak terus termasuklah ciri-ciri di peringkat molekular, zarah dan serbuk serta sifat-sifat kefungsiannya di dalam formulasi tablet Paracetamol cetak terus. Analisis spectrum FT-IR dan ^{13}C-NMR menunjuk bahawa pragelatinasi tidak mengubah struktur kimia kanji sagu. Corak XR-D kanji sagu menunjukkan ciri-ciri jenis-C manakala PS mempamerkan jenis-A dan darjah pengkristalan berkurang apabila masa pemanasan ditingkatkan. Keluk DSC menunjukkan pragelatinasi meningkatkan suhu gelatinasi (T_o), suhu maksima (T_p) dan darjah gelatinasi (DG), mengecilkan jarak suhu gelatinasi ($T_c - T_o$) dan mengurangkan entalpi peleburan (ΔH) kanji sagu, kesannya menjadi lebih ketara apabila masa pemanasan ditambahkan. Pemerhatian SEM menunjukkan semakin banyak granul kanji sagu tidak lagi mempunyai permukaan yang licin dan berbentuk tidak teratur bermunculan dengan bertambahnya masa pemanasan. PS menunjukkan lebih tinggi kuasa pengembangan (SP) pada suhu $\leq 55^{\circ}$C dan indeks kelarutan dalam air (WSI) pada suhu $\leq 65^{\circ}$C berbanding kanji sagu. Masa pemanasan yang lebih panjang menghasilkan PS dengan kandungan amylosa yang lebih rendah dan kelikatan, SP dan WSI yang lebih tinggi. Penilaian pengaliran serbuk dan analisis kompak serbuk menggunakan persamaan Heckel dan Kawakita, sifat-sifat mekanikal dan sensitiviti pelinciran mendedahkan bahawa pragelatinasi meningkatkan pengaliran, kebolehmampatan dan sensitiviti pelinciran kanji sagu, mengikuti turutan PS4>PS3>PS2>PS1>kanji sagu. Pengaliran, kebolehmampatan dan kebolehkompakan PS4 adalah setanding dengan Spress® B820 tetapi menunjukkan sensitiviti pelinciran yang lebih rendah. Berbanding dengan Avicel PH 101, pengaliran PS4 adalah lebih baik

tetapi kebolehmampatan, kebolehkompakan dan sensitiviti pelincirannya adalah lebih rendah. Berdasarkan pada penemuan kajian, PS4 merupakan calon terbaik di antara PS sebagai eksipien cetak terus. Penilaian kapasiti muatan untuk Avicel PH 101, PS4 dan Spress® B820 berbanding dengan Paracetamol kurang mampat masing-masing mencapai 70.16%, 60.97% dan 59.16% w/w. Tablet Paracetamol yang diformulasikan dengan Avicel PH 101 (Formulasi 1) menunjukkan masa pengecaian terpantas, diikuti oleh tablet yang diformulasikan dengan PS4 (Formulasi 3) dan Spress® B820 (Formulasi 2), ketiga-tiganya dengan masa pengecaian kurang daripada 2 minit, ini menunjukkan sifat pengecaian yang baik. Walau bagaimanapun, Formulasi 1 tidak melepaskan 80% Paracetamol dalam masa 30 minit sepertimana yang dikehendaki oleh USP 27. Profil disolusi untuk Formulasi 2 dan 3 adalah serupa; kedua-duanya melepaskan > 80% Paracetamol dalam masa 20 minit dan melepaskan Paracetamol sepenuhnya dalam masa 25 minit. Penambahan Avicel PH 101 dan kanji sodium glycolate ke dalam Formulasi 2 dan 3, dikenali sebagai Formulasi 4 dan Formulasi 5, menunjukkan perpendekan masa pengecaian yang ketara dan > 80% Paracetamol dilepaskan dalam masa 5 minit. Formulasi 4 dan 5 masing-masing melepaskan 100% dan 99.95% Paracetamol dalam masa 15 minit. Kecekapan disolusi kedua-duanya berbeza sebanyak 0.19%, menunjukkan profil disolusi dan kesetaraan-bio yang serupa. Keputusan kajian kestabilan yang dipercepatkan pada 40 ± 2°C / 75 ± 5% RH dengan masa penyimpanan selama 3 dan 6 bulan menunjukkan Formulasi 4 dan 5 adalah stabil. Sebagai kesimpulan, kajian ini mendapati bahawa PS4 mempunyai potensi sebagai eksipien cetak terus, ciri-ciri dan prestasinya adalah setanding dengan Spress® B820.

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LIST OF SYMBOLS & ABBREVIATIONS

C	apparent crystallinity (%)
DG	degree of gelatinization
ΔH_p	enthalpy of pregelatinised sago starch
ΔH_n	enthalpy of native sago starch
W_w	weight of wet sediment
W_d	weight of dried sediment
ε	porosity of a powder
ρ_T	true density
ρ_0	bulk density
ρ_t	tapped density
α	angle of repose (°)
D	relative density of a powder compact at applied pressure
P	compression pressure
ρ_A	apparent density
T	tensile strength
T_o	onset temperature
T_p	peak temperature
T_c	conclusion temperature
ΔH	melting enthalpy

LIST OF APPENDICES