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Compaction and Compressibility Characteristics of Modified Starches Derived from *Plectranthus Esculentus b*y Direct Compression

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ABSTRACT

In this study, the compactability and compressibility of modified starches obtained from the tuber *Plectranthus esculentus* were evaluated in comparison with the standard microcrystalline cellulose (MCC 101). Starch was extracted from the fresh tubers of *P. esculentus* by wet milling. Three modifications of the starch were made, acid hydrolysis (APS), pregelatinization (PPS), and ethanol dehydrated pregelatinization (PPE). Tablet's compaction characteristics were studied using models of Heckel and Kawakita equations, while compressibility index were evaluated using tablet's density measurements. The percentage recovery yields for the three modifications revealed that PPS has the highest yield in comparison to PPE and APS. Compaction and compressibility evaluation demonstrate that modification by acid hydrolysis (APS) and ethanol dehydration of the pregelatinized starch (PPE) produced directly compressible filler/binder that can plastically deform on compression base on their mean yield pressure P_y and the inverse measure of plastic deformation P_k values were lower in comparison to the pregelatinized modification (PPS). Compressibility index also revealed that APS and PPE are more compressible and better comparable to mcc 101 than PPS.

Keywords: Compaction, compression, starch, microcrystalline cellulose, Heckel and Kawakita equations.

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INTRODUCTION

Starch is composed of very small spherical or elliptical granules. It is colorless, odorless with slight characteristic taste. In pharmaceutical manufacture, starch is an important excipient that has been commonly employed because of its versatility and cheapness [10]. Native starches were well explored as binder and disintegrant in solid dosage forms, but due to poor flowability their utilization is restricted. Most common form of modified starch i.e. Pregelatinized starch marketed under the name of starch1500 are now most preferred directly compressible excipients in pharmaceutical industry. Other modifications include acid hydrolysis, enzyme hydrolysis and various forms of chemical modification [13]. Recently modified rice starch, starch acetate and acid hydrolyzed diascorea starch were well established as multifunctional excipients in pharmaceutical industry[3].

Livingstone potato (*Plectranthus esculentus*), is among the non-popular African tubers, it was first identified by N.E. Brown in 1894. The plant is a yellow-flowered member of the mint family (Lamiaceae) with elongated tubers. It is a dicotyledonous perennial shrub cultivated for its edible tubers which contains reasonable quantity of carbohydrates as source of energy especially in the rural areas[19]. It is indigenous to tropical Africa. It was also first cultivated in the Upper Niger valley of the Hausaland in Nigeria and in the Central African Republic [20].

Powder could be considered as a disperse system, where particles (the solid phase) are dispersed in air (the gas phase). The term powder compression describes the volume reduction of a powder bed in a confined space caused due to application of pressure. Hence, the compressibility describes the ability of a powder to decrease in volume when pressure is applied. When a powder is compressed, the gas-phase is reduced and the particles are brought closer to each other. The interparticulate bonds become stronger and finally the bulk powder transforms into a coherent compact [6].

Several views regarding the mechanism of the powder compression process exist, but the description of it as a process occurring as a sequence of event or stages is considered the most common [7]. Each stage represents a certain part of the pressure range used, and is associated with one or more dominating compression mechanisms. However, four main stages are involved comprising initial particle rearrangement, particle fragmentation, particle plastic deformation and finally elastic deformation of the compact [5].

Compaction is a result of compression and cohesion properties of a powder. It is the formation of solid specimen of defined geometry by powder compression[2]. The common approaches used to depict powder compression have been to take the whole powder bed or tablet into consideration

during modeling (global models), by relating either the powder porosity or the powder volume to the applied pressure[14].

The Heckel equation is based on the measurement of tablet porosity on an ejected tablet or on a powder column under load. The equation is the most commonly used. The equation is based on the assumption that compression of powders is analogous to a first-order chemical reaction, the pores being the reactant and densification of the bulk being the product. Base on this assumption, the following expression was derived:

$In\ (1/e) = KP + A$……. (1)

Where *e* is the porosity of the powder bed and *P* the applied compression pressure, *A* is constant suggested to reflect particle rearrangement and fragmentation, and *K* the slope of the linear part of the relationship which is suggested to reflect the deformation of particles during compression. The reciprocal of the slope value *(1/K)* often calculated and it represents the yield stress or yield pressure *(Py)* for the particles, i.e

$In\ (1/e) = (P/Py) + A$…… (2)

The yield stress is defined as the stress at which plastic deformation of a particle is initiated. Experimental conditions must be kept constant for appropriate comparison of heckle parameters [18]

The value of *e* can be generated from the powder bed's relative density (*D*), and is given by the equation:

$e = 1/1-D$…… (3)

From the value of intercept *A*, the relative density D_A can be calculated using the following relation:

$D_A = 1- e^{-A}$..... (4)

D_0 is the relative density at zero pressure, it is the ratio of the material's loose (bulk) density to its particle density. D_B describes the phase of rearrangement at low pressures, and is given as follows:

$D_B = (D_A – D_0)$ …….. (5)

Another way of representing compression data is to relate the volume reduction of a powder bed to the applied pressure, and the most familiar expression in this class is the Kawakita equation [9]. This was derived from the assumption that, during powder compression in a confined space, the system is in equilibrium at all stages, so that the product of a pressure term and a volume term is constant. The equation can be written in the following linear form:

$P/C = P/a + 1/ab$…….. (6)

Where C is the degree of volume reduction and is given by the expression:

$C = (V_o - V)/V_o$ ..... (7)

V_o is the initial volume of the powder bed and V is the volume under applied pressure, P is the applied pressure, and a and b represent the minimum porosity before compression and material plasticity respectively. The linear relationship between P/C and P makes it possible to derive values of the parameters a and b. and mathematically the parameter b is equal to the reciprocal of the pressure (P).

MATERIALS AND METHOD

Materials

Experimental starch was processed in the Department of Pharmaceutics and Pharmaceutical Microbiology of Ahmadu Bello University-Nigeria. Other materials used in this research were all of pharmaceutical grade: Absolute ethanol (Emerck Darmstadt, Germany), hydrochloric acid (Emerck Darmstadt, Germany), microcrystalline cellulose PH 101 (ATOZ Pharmaceuticals Ltd, Ambaltur, India), xylene (Loba Chemic Laboratory Ltd, Mumbai India), sodium hydroxide pellets (Avondale Laboratories Ltd, Banbury, England), magnesium stearate (BDH Chemicals Ltd Poole, England) and distilled water.

METHODS

Collection, Identification and Extraction of *Plectranthus esculentus* Starch

Fresh tubers of *Plectranthus esculentus* (N.E. Brown) were obtained from Bom area of Riom Local Government Area of Plateau state, Nigeria. The tubers were identified in herbarium of the Department of Biological Sciences, Ahmadu Bello University, Zaria, Nigeria. (Voucher number 28448)

The tubers were brought to the Process Laboratory of the Department of Pharmaceutics and Pharmaceutical Microbiology of Ahmadu Bello University, Zaria, washed, peeled and grated. The grates were washed and weighed, this was then grinded to fine pulp using grinding machine. Calico cloth was used to sieve the pulp with sufficient distilled water which aided the separation of the starch from chaff. The starch in the excess water was allowed overnight. The supernatant was decanted and little quantities of 0.1N sodium hydroxide (NaOH) solution was added and stirred for about 10 minutes to dissolve the protein contents. The suspension was then centrifuged at 1000 rpm for 10 minutes. The starch obtained was spread on stainless steel trays and air-dried for 24 hours and then dried in hot air oven (BS size 3, Gallenkamp, England) at 40^0 C for one hour. The dried starch was size-reduced to fine powder using mortar and pestle. It was weighed and

percentage yield determined. This was then packed in a polythene bag, labeled and stored at room temperature until required.

Identification test for Starch

This was done according to British Pharmacopeia [4] specification. One gram (1 g) of the starch sample was suspended in in 50 mL distilled water and boiled for a minute and cooled. A drop of iodine solution was added to 1 mL of the starch mucilage formed and observed the color change

Preparation of Acid Hydrolyzed *Plectranthus esculentus* Starch

Three hundred grams (300 g) of the native starch powder was suspended in 805.3 ml of distilled water. The reaction was initiated by adding 28 mL of 6 N HCl into the suspension and stirred and placed on digital thermostatic water bath (McDonald Scientific International, Lagos, Nigeria) set at 52^0 C and the reaction was allowed to proceed for 24 hours while stirring intermittently. Equal volume of distilled water was added at room temperature and centrifuge at 1000 rpm for 10 minutes. The pH was then adjusted with 1 N NaOH, sufficient quantity of water was added again and then dehydrated with 95 % ethanol. Hydrolyzed starch was spreads on stainless steel tray and air dried for 24 hours, then dried in hot air oven at 40^0 C for 1 hour. Percentage wield was determined and starch labeled APS.

Preparation of pregelatinized *Plectranthus esculentus starch*

One hundred and fifty grams (150 g) of the native starch powder was weighed on electronic digital balance and transferred into a stainless steel bowl; 1.0 L of distilled water was added at room temperature and stirred to form suspension. The suspension was placed on water bath (Digital thermostatic water bath) set at 90^0 C and stirred the suspension continuously until it gelatinized at 66^0 C. the mucilage was then thinly spread on stainless steel trays and dried in hot air oven at 60^0 C for 24 hours. The dried flakes were milled using laboratory blender. This was labeled pregelatinized *P. esculentus* starch (PPS), and the percentage yield was determined using the equation below

$$P_y = P/P_o X\ 100 \quad \ldots\ldots (8)$$

Where,

P_y is the percentage yield, P is the weight of the pregelatinized starch formed and P_o is the initial weight of the native starch powder used. This procedure was repeated but instead of drying directly, absolute ethanol was used to dehydrate the starch, and then dried at 40^0 C for 24 hours, milled and labeled as ethanol dehydrated pregelatinized *P. esculentus* starch (PPE).

Determination of Particle Density

The particle densities (ρs), of the samples were determined by the liquid displacement method using xylene as the immersion fluid and computed according to the following equation:

$\rho s = Wp\ [(a + Wp) - b]\ x\ SG$……(9)

Where, Wp is the weight of powder, SG is specific gravity of solvent (xylene, 0.86), a is weight of bottle + solvent and b is weight of bottle + solvent + powder.

Determination of Bulk and Relative Density

Ten grams (10 g) powder was poured at an angle of 45^0 through funnel in to a 50 mL measuring cylinder of diameter of 22 mm and the bulk volume noted. The bulk density (BD) was then calculated. The measurement was repeated three times. The relative density (D_O) of each material was calculated as the ratio of the loose (bulk) density to its particle density.

Compaction Studies and Determination of Compressibility Index

Compacts of each powder sample were made by weighing 500 mg individually and compressed at various compression loads ranging from 28.31 – 169.88 MNm^{-2} on Apex hydraulic hand press (Model 184, Apex Construction Ltd., London W.I and Dartford). The dwell time of 30 seconds was allowed for each compression. Before the compression, the 10.5 mm die and flat-faced punches were lubricated with 2 % w/v dispersion of magnesium stearate in acetone solution. After ejection, the compacts were stored in a desiccator over silica gel for 24 hours to allow for elastic recovery and hardening and also to prevent low yield values. The tablet weights (W) and dimensions (thickness and diameter) were then determined to within ± 1 mg and ±0.01 mm respectively and their relative densities (D) were calculated using the following equation:

$D = W/V\rho s$……. (10)

Where, V is the tablet volume (cm^3) and ρs is the particle density (g/cm^3) of the solid material. Heckel plots of ln (1/1-D) against the applied pressure P (MNm^{-2}) and Kawakita plots of P/C versus P were constructed for all the materials. Also compressibility index was determined using plot of compact density (g/cm^3) versus log compaction load (MNm^{-2}).

Statistical Analysis

Data were presented as mean ± standard error of mean (SEM). Differences between means were analyzed by one way analysis of variance (ANOVA) , followed by Dunett's test for multiple comparison using the IBM SPSS version. Significant differences among means were considered at 95 % confidence level and $p \leq 0.05$.

RESULTS AND DISCUSSION

As presented in Table 1, the percentage yield of the *P. esculentus* starch was 31.67 % w/w and this is averagely fair for tubers [10]. The gelatinization temperature was found to be 66^0 C, and it tests positive to iodine test confirming that it is starch. The percentage recovery yields for ethanol dehydrated pregelatinized starch, pregelatinized starch and acid hydrolyzed starch were presented in Table 2. The order is PPS>PPE>APS. APS has the lowest percentage recovery yield, this could be connected to the fact that reaction of the starch in 6 N HCl was allowed to proceed for 24 hours, and the more time spent during the reaction the more by-products are produced [17]. Loss may also result due to removal of ash and color by several washing [16].

Table 1, Organoleptic and Physical Tests on Native Starch of *P. esculentus*

Properties	Result
Taste	Tasteless
Odor	Odorless
Color	White
Texture	Smooth
Gelatinization temperature ^{0}C	66
Percentage yield (% w/w)	31.67
Iodine test	Positive

Table 2, Physical Tests of Modified Starches of *P.esculentus*

Properties	PPE	PPS	APS
Color	Off white	Light brown	Off white
Texture	Brittle	Brittle	Smooth
Recovery yield (% w/w)	89.54	90.61	76.74

***Key:**

APS= Acid hydrolyzed *Plectranthus esculentus* Starch

PPS= Pregelatinized *Plectranthus esculentus* Starch

PPE=Ethanol dehydrated Pregelatinized *Plectranthus esculentus* Starch

Table 3, Physicochemical Properties of Modified Starches of *P. esculentus* and MCC 101 (Mean ±SEM)

Parameter	MCC 101	PPE	PPS	APS
Bulk Density (g/cm^3)	0.34 ± 0.00	0.66 ± 0.01	0.73 ± 0.02	0.64 ± 0.01
Particle Density (g/cm^3)	1.82	1.42	1.71	1.91

Figure 1, shows the Heckel plots of modified starches of *P. esculentus* and MCC 101. The mean yield pressure P_y was calculated from the regions of the plots showing the highest correlation coefficient of ≥0.99 for all the formulations. The intercept A was determined from the extrapolation of the linear line. The values for P_y, D_0, D_A, and D_B for the formulations are

presented in Table 4. The mean yield pressure, P_y, is inversely related to the formulations ability to deform plastically under pressure [12]. The *Py* values showed that MCC 101 has the lowest while APS exhibited the highest. This finding indicate plastic deformation of these materials in the following order MCC 101>PPE>PPS>APS. This simply indicates that MCC 101 is still superior in terms of plastic deformation in comparison to the various starches used in this study.

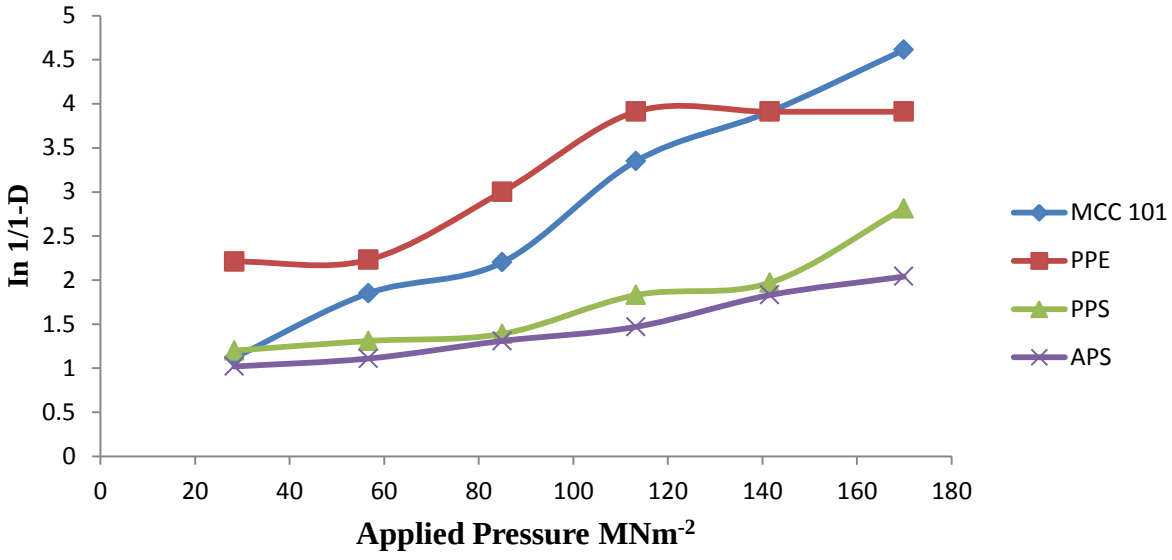

Figure 1. Heckel plots for MCC 101, PPE, PPS and APS of compact materials alone

The D_0 value represents the degree of initial packing in the die as a result of die filling. This result indicates that PPE exhibited a high degree of packing followed by PPS, with MCC 101 having the lowest initial packing. This could be related to the low bulk density of MCC 101.

The D_A values, which represent the total degree of packing at zero and low pressures, PPE was shown to have the highest value while MCC 101 exhibited the lowest D_A value. The ranking was PPE>APS>PPS>MCC 101.

The D_B value represents the particle rearrangement phase in the early compression stages and tends to indicate the extent of particle or granule fragmentation, although fragmentation can occur concurrently with plastic and elastic deformation of constituent particles [12]. The D_B values were PPS<MCC 101<APS<PPE. This result indicates that PPE requires least pressure to undergo fragmentation and rearrangement while PPS may require high pressure because it has the least D_B value.

Figure 2, represent the Kawakita plots and the various Kawakita parameters were displayed in Tablet 4. A linear relationship was attained at all compression pressure with a correlation coefficient value of 0.999 for all materials. The Kawakita parameters were generated from the

slopes and intercepts from the plots. a and b values were obtained from the slope and intercepts of the plots respectively. 1-a provides the values for initial relative density $D_{I,}$ while P_k values were generated from the reciprocal of b (Table 4.).

Table 4, Parameters for Heckel and Kawakita Plots

Material	Heckel Parameters				Kawakita Parameters			
	Py	***D_0***	***D_B***	***D_A***	***a***	***b***	***D_I***	***P_k***
MCC 101	40.00	0.19	0.12	0.30	0.857	0.095	0.143	10.526
PPE	68.49	0.47	0.36	0.83	0.637	0.063	0.363	15.873
PPS	94.33	0.43	0.08	0.51	0.594	0.043	0.406	23.256
APS	133.33	0.34	0.18	0.52	0.669	0.058	0.331	17.241

*P_y is the mean yield pressure; D_0 is the relative density at zero pressure; D_A is the relative density from the value of intercept *A*; D_B describes the phase of rearrangement at low pressures ($D_A - D_0$); a is the minimum porosity before compression; b represent plasticity; D_I is the initial relative density and P_k is the inverse measure of plastic deformation (reciprocal of *b*).

Table 5, Compressibility index of MCC 101 and modified starches of *P. esculentus*

Excipient	Slop (Compressibility)
MCC 101	0.992
PPE	0.478
PPS	0.503
APS	0.691

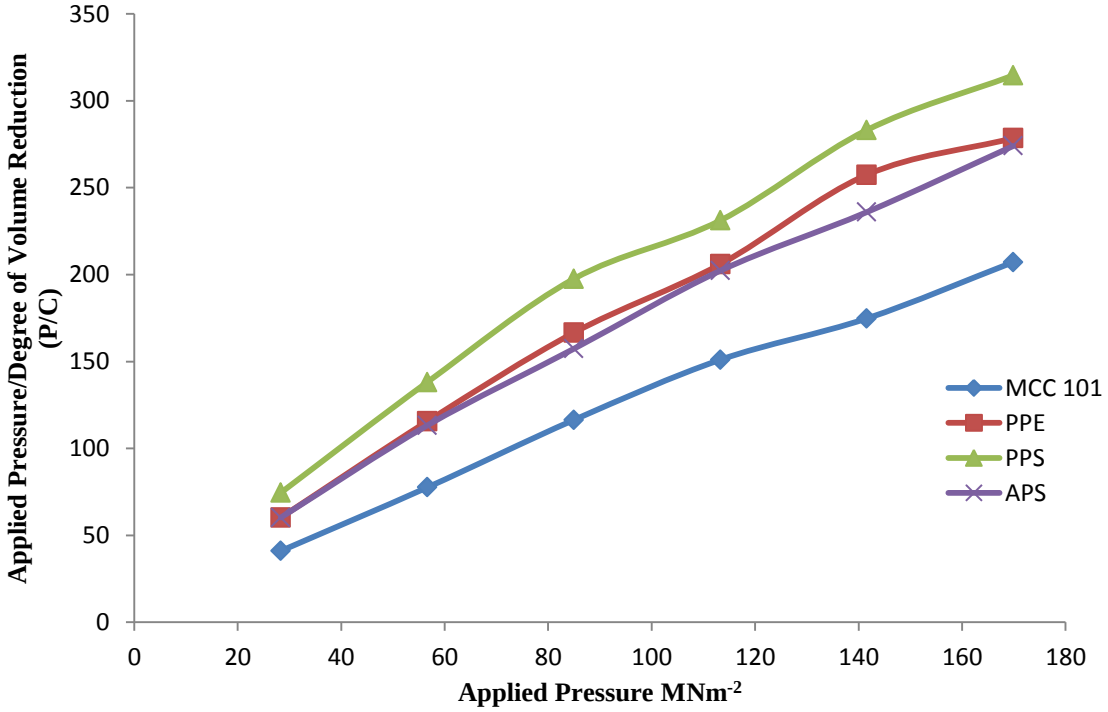

Figure 2. Kawakita plots for MCC 101, PPE, PPS and APS of compact materials alone

The D_I values, which is a measurement of the packed initial relative density of the starches with the application of small pressures or tapping [11.] The values decrease in the following order; PPS>PPE>APS>MCC 101. The order of the results confirmed what was observed in Heckel plots were MCC 101 exhibited a lowed value for loose initial relative density D_0 in comparison to the modified starches. A similar finding was reported from microcrystalline starch obtained from *Manihot esculenta* [1]

The P_k values, which are an inverse measurement of the plastic deformation occurring during the compression process [11]. This simply means that the lower the value, the higher the degree of plastic deformation occurring in a material. The values are ranked as follows; MCC 101<PPE<APS<PPS. This ranking also followed the same pattern with what was observed in Heckel plots where MCC 101 also exhibited the lowest value for P_y indicating higher plastic deformation. Thus, from this result, it can also be said that among the modified starches PPE exhibited the highest plastic deformation, followed by APS and then least by PPS. It has been found that the higher the plastic deformation a material undergoes the more contact points created for interparticulate bonding to occur during compression [8]. Thus, formulations with PPE and APS Could produce tablets with better mechanical strength than PPS.

Compressibility Evaluation

Compressibility simply means the ability of a material to reduce in volume when compression pressure is applied to it. A linear relationship exists between the density of tablets and the logarithm of compaction pressure [15]. The rate of increase of tablet density with increasing compaction pressure could be considered as an expression of compressibility [15]. The value of slope from the plot of tablet density versus log of compression pressure is considered to express the compressibility index of a material, the bigger the value the better the compressibility of the material. These values were displayed in Table 5 as obtained from Figure 3, and it follows the following ranking MCC 101>APS>PPS>PPE. This result shows comparable increase in density of tablets with increase compression pressure of MCC 101 with APS and PPS, but PPE exhibited the lowest value, indicating lower compressibility.

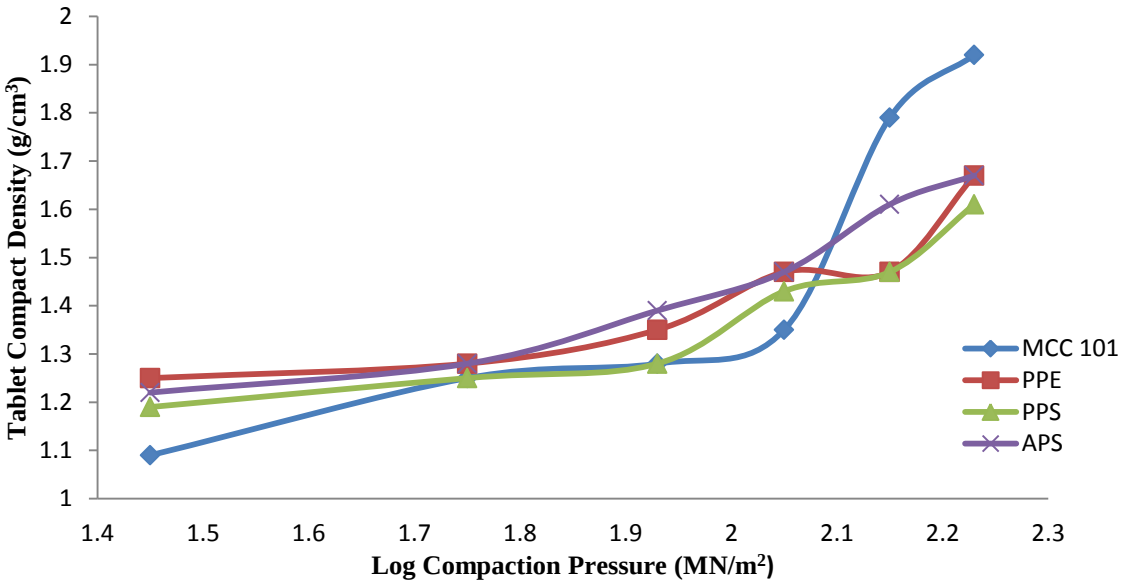

Figure 3. Plots of tablet compact densities of MCC 101, PPE, PPS and APS against log pressure

CONCLUSION

Modification by acid hydrolysis (APS) and ethanol dehydration of the pregelatinized starch (PPE) can produce directly compressible filler/binder that can plastically deform on compression because their P_k and P_y values were lower and comparable to that of MCC 101 than the pregelatinized modification. Compressibility indices also revealed that APS and PPS are more compressible than PPE. Hence, this study revealed that modified starches of *P. esculentus* could be useful as direct compression filler/binder in tablet formulation with good mechanical properties.

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