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Research Paper

Formulation and Evaluation of Co-processed Acacia Gum and Potato Starch

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ABSTRACT: *Acacia gum and potato starch do not always provide the required performance for active pharmaceutical ingredient to be formulated or manufactured by direct compression due to poor flow properties and dilution potential, hence it is necessary to co-process the two excipients that is, acacia gum and potato starch. hence this study. Acacia gum was co-processed with potato starch at varying ratios (0.5:49.5, 0.75:49.25, 1:49, and 1.25:48.75) in a co-solvent system consisting of acetone and distilled water (2:1). The physical properties of the excipients were studied using standard methods. Tapping experiment was used to study the consolidation properties of the excipients. The volume of reduction was estimated using the Kawakita equation. Co-processed acacia gum and potato starch Batch D (1.25: 48.75) was found to give the best physical properties with bulk, tapped density and Hausner ratio of 0.487 g/cm^{3}7,0.566 g/cm^3, and 1.16 respectively. It also gave angle of repose of 26.7 º. In conclusion, Acacia gum co-processed with potato starch can serve as a locally sourced alternative to costly commercially available directly compressible excipients.*
KEYWORDS: *Acacia gum, potato starch, co-processed excipients, binary mixtures, physical properties*

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I. INTRODUCTION

Co-processing is a particle engineering technique that combines two or more excipients at the sub-particle level with the aim of improving the functionality of the final product while minimizing the short-comings of the individual excipients [1] and [2]. With co-processing, pharmaceutical manufacturers have the option of using a single excipient with multiple functional properties, thereby reducing the number of excipients in inventory.

Development of a co-processed excipient involves identifying two or more excipients to be co-processed by studying material characteristics and functionality requirements, selecting the proportions of excipients to optimize, assessing a suitable solvent in which to disperse the excipients, selecting an appropriate drying process and optimizing the process to avoid batch-to- batch product variations. Co-processed excipients have the advantage of a higher dilution potential, that is, the ability of the excipient to retain its compressibility when diluted with another material; than a physical mixture of its constituent excipients [3], In addition, they have improved flow properties and improved compressibility profiles than the individual excipients. Also, studies have shown that after co-processing, the chemical properties of the individual excipients may not show any chemical change as no covalently bonded chemical entity is formed when the individual ingredients are combined to form the co-processed excipients [4]. The co-processed excipients are introduced to achieve a better flow, better dilution potential, and reduced fill weight variation in comparison with a single substance or the physical admixture. Several of these excipients are commercially available. Examples include Avicel CE-15 (microcrystalline cellulose and guar gum), Avicel HFE-102 NF, Cellactose 80 (lactose-cellulose), Ludipress (lactose, polyvinylpyrrolidone, and crosspovidone), and Prosolv (microcrystalline cellulose and silicon dioxide) [5],[6],[7], and [8].

A tablet is a solid dosage drug form. It comprises of mixture of active pharmaceutical ingredient and excipients, usually in granules, pressed or compacted from powder to a solid dose. They are of various shapes; oval, square, round, octagonal, and so on and with convex, flat or other form of upper and lower surface. Tablets are manufactured by mainly three techniques: wet granulation, dry granulation and direct compression. In wet granulation and dry granulation techniques, various processing steps and manufacturing challenges are involved, leading to higher cost and time of tablet production. In contrast to this, the direct compression technique involves simply the compression of dry blend of powders that comprises the drug and various excipients. The simplicity

and cost-effectiveness of the direct compression process have positioned it as a preferred alternative. Direct compression is the most popular because it provides the shortest, most effective and least complex way to produce tablet [9], but it has been estimated that less than 20 percent of the pharmaceutical materials can be compressed directly into tablets. Direct compressible excipients are the special products produced by patented spray drying, fluid bed drying, roller drying or co-crystallization. Hence the products are relatively costly than the respective raw materials. In response to these deficiencies, it is necessary to co-process two excipients such as acacia gum and potato starch which is expected to possess performance advantages that cannot be achieved using a physical admixture of the same combination of these two excipients.

II. MATERIALS AND METHODS

Potato starch powder (Central Drug House (P) Ltd., India), Acacia gum powder (Loba Chemie PVT. Ltd., India), Avicel®CE 15, Avicel® HFE-102 NF, Cellactose® 80 (gifts from Katchey Company Ltd, Lagos, Nigeria).

2.1 Preparation of Co-Processed Acacia Gum and Potato Starch

A 50 g acacia gum and potato starch mixtures at different ratios, (0.5 :49.5, 0.75 :49.25, 1 :49, 1.25 :48.75) were co-processed respectively. Acacia gum powder and potato starch powder were mixed in a dry porcelain mortar using doubling up technique and the mixture of acetone and water in ratio 2:1 respectively was added to form a wet coherent mass, which was then passed through mesh no 22 to obtain wet granules. The granules were then dried in an oven at 50 ℃ for 90 min. The dried granules were dry screened using mesh no 7. The granules obtained was then stored in a tightly closed glass bottle.

Table 1: Formulae for preparation of batches of co-processed excipient

Materials	Batch Ratios			
	A	B	C	D
Acacia gum (g)	0.5	0.75	1	1.25
Potato Starch (g)	49.5	49.25	49	48.75

2.2 Determination of particle size and shape

Acacia gum powder, potato starch powder, co-processed excipient Batch D (1.25: 48.75) (selected based on best performance), its physical admixture, avicel® CE 15, avicel® HFE-102 NF, and cellactose® 80 particle size and shape were determined using optical microscope (LEICA Galen III Research Microscope, USA) equipped with an integrated camera (Celestron digital microscope imager, model 44421, USA). 300 particles were randomly selected from the optical field. Photomicrographs of the powders taken were analyzed using Image-J software (Model 1.48v, Wayne Rasbond, USA). The size and shape descriptors are as shown below:

Aspect ratio = b/l (1)

Roundness = $4\pi\ A/P^2$ (2)

Irregularity =p/l (3)

Equivalent circle diameter (ECD) = $\sqrt[2]{A/\pi}$ (4)

Elongation ratio = l/b (5)

Where:

b=length of minor axis (minimum Ferret diameter)

l=Length of major diameter (maximum Ferret diameter)

A= Projected area of the particle

p= Perimeter of the particle

2.3 Measurement of the Bulk Densities of the Excipients

A 30 g of each excipient, namely, potato starch, acacia powder, co-processed excipients (avicel® CE 15, avicel ® HFE-102 NF, cellactose®80, and Batch A to D), and the physical admixture of the best batch (Batch D) was weighed and poured into a dry 100 ml measuring cylinder of known diameter at angle 45 º. The height occupied by each excipient at zero pressure was noted and recorded.

This experiment was performed in triplicate and the average reading was recorded. The bulk density was calculated as the weight per unit volume of the excipient.

Where: Bulk density = $\frac{weight}{bulk\ volume}$ (6)

The bulk volume was calculated using the formula $V_o = \pi r^2 h$

Where;

V_o =bulk volume

R = Radius

H =Height

2.4 Measurement of Tapped Density of the Excipients

A 30 g of each excipient, potato starch, acacia gum and the co-processed excipients (avicel® CE 15, avicel ® HFE-102 NF, cellactose® 80, Batch A to D), and physical admixture of batch D of the above whose bulk height has been noted at zero pressure was then subjected to 20,40,60,80 and 100 taps on a soft padded table surface. The height occupied by each excipient was measured and recorded.
This experiment was performed in triplicate and the average reading was determined. The tapped density at 100 taps was calculated as the weight per unit volume of the excipients
Where;

$$\text{Tapped density} = \frac{weight}{tapped\ volume} \quad (7)$$

The tapped volume V_{100} was calculated using the formula $V_{100} = \pi r^2 h$
Where
V_{100} = tapped volume
r =radius of the measuring cylinder
h = height occupied by the excipient at 100 taps

Carr's compressibility index
This was calculated using the equation

$$CI = \frac{tapped\ density - bulk\ density}{tapped\ density} x\ 100 \quad (8)$$

Hausner's ratio (%)
This is the ratio of the tapped density to bulk density

$$HR == \frac{tapped\ density}{bulk\ density} \quad (9)$$

2.5 Measurement of Angle of Repose of the Excipients

A 20 g sample of potato starch, acacia gum and the co-processed excipients, (avicel® CE 15, avicel® HFE-102 NF, cellactose 80, Batch A to D), and physical admixture of batch D was passed through a conical funnel which was clamped on a retort stand such that the perpendicular height of the tip of the funnel was 5 cm from the flat table surface. A plain clean sheet paper was placed under the funnel. The height of the heaped formed was measured as h(cm). The diameter of the circumference of the heap was divided to the radius r. The experiment was performed in triplicate and the average was recorded
The angle of repose was calculated using the equation below:

$$\emptyset = \tan^{-1} \frac{h}{r} \quad (10)$$

Where :
H= height of the powder cone (cm)
R= radius of the cone base (cm)

2.6 Determination of Packing and Cohesive Properties of Excipients

These were determined by pouring 30 g of each excipient namely acacia gum, potato starch, co-processed excipients of Batches A to D, and the physical admixture of the batch with the best flow property (1.25:48.75), avicel® CE 15, avicel® HFE-102 NF and cellactose®80 into a 100 mL measuring cylinder of known diameter. The measuring cylinder was held with hand like a fulcrum at a distance of 4.5 cm away from the surface, on a soft padded surface. The height at 20, 40, 60, 80 and 100 taps were noted and recorded. The tapped height noted and tapped density calculated.
The volume was calculated using the formula $v=r^2h$, where
v= tapped volume
r= radius of the measuring cylinder
h= height of the excipient in the cylinder at 100 taps
The packing and cohesive properties of each excipient were determined from modified Kawakita equation:

$$N/C = N/a + 1/ab \quad (11)$$

From the plot of a graph of N/C against N, constants a and b were determined. Where a and b are constants; 'a' is the maximum volume of reduction of powder bed of each excipient, which is the reciprocal of the slope of the graph, i.e, a=1/slope while 'b' is the index of compressibility. This implies that the intercept of the graph= 1/ab. N is the number of taps; C denotes the volume of reduction which can be calculated according to the equation:

$$C = \frac{Vo - Vn}{Vo} \quad (12)$$

Where V_o and V_N are the powder bed volumes at initial (bulk volume) and nth tapped states respectively [10].

2.7 Determination of Consolidation Index and Rate of Consolidation

These were determined by using the method described by Alebiowu and Adeoye [10] was used to study the relative decrease in powder volume and density change as a function of applied load.

$$\text{Log } \{(p_{td} - p_{bd}) / p_{td}\} = K \log N + C \quad (13)$$

where K and C are constants denoting the rate of consolidation and consolidation index, respectively, N is the number of taps, while p_{bd} and p_{td} are bulk density and the tapped density of the powder bed after Nth tap, respectively. Graph of Log $(p_{td} - p_{bd} / p_{td})$ against log N was plotted for acacia gum, potato starch, co-processed excipients of batches A to D, and the physical admixture of the batch with the best flow property (1.25:48.75), avicel® CE 15, avicel® HFE-102 NF and cellactose® 80.

2.8 Determination of Porosity of Excipients

This is a calculation from the results of bulk density (loose density) and particle density of the excipients namely acacia gum, potato starch, co-processed excipients of batches A to D, and the physical admixture of the batch with the best flow property (1.25:48.75), avicel® CE 15, avicel® HFE-102 NF and cellactose®80.

First, the relative density (RD) of each excipient was calculated from the equation:

RD = Bulk (loose) Density/Particle Density

Then, Porosity = 1- RD (14)

III. RESULTS AND DISCUSSION

3.1 Particle Size and Shape of Excipients

The particle size and shape of the excipients are presented in Table 2. Aspect ratio of a geometric shape is the ratio of its sizes in different dimensions. Roundness is a measure of how closely the projected area of the powder resembles a circle with a perfect circle having a roundness of 1. Irregularity measures the surface area compared to the size of the particle with a perfect circle having an Irregularity of 3.142. Equivalent circle diameter is a measure of size, it is diameter of a sphere with the same cross-sectional area of the powder. Co-processed excipient Batch D gave the highest equivalent circle diameter. The higher the equivalent circle diameter, the larger the mean particles [10] and [11].

Table 2: Particle size and shape of excipients

Excipients	Elongation ratio	Roundness	Irregularity	Equivalent circle diameter (um)
Acacia gum	0.11	1.01	1.96	2.26
Potato starch	0.04	0.81	2.16	2.76
Physical admixture Batch D	0.04	0.81	2.16	2.76
Co-Processed Batch D	0.05	0.63	2.32	4.22
Avicel CE 15	0.01	1.57	2	1.13
Avicel HFE-102 NF	0.02	1.08	2.16	1.59
Cellactose 80	2.24	1.39	1.89	1.59

Table 3: Physical properties of excipients

Parameters	Potato starch	Acacia gum	Avicel CE 15	AvicelHFE-102	cellactose 80	Physical admixture Batch D
Bulk density (g/cm^3)	0.535± 0.14	0.633±0.29	0.468±0.22	0.343±0.41	0.416±0.48	0.553±0.09
Tapped density (g/cm^3)	0.812± 0.38	0.878±0.29	0.695±0.07	0.477±0.15	0.523±0.31	0.738±0.05
Carr's index (%)	34.11	27.90	32.66	28.09	20.4	25.07
Hausner Ratio	1.52	1.39	1.49	1.39	1.26	1.33
Angle of repose (°)	44.4±0.25	41.5±0.12	47.3±0.1	44.0±0.12	36.1±0.12	39.6±0.2

Table 4: Physical properties of co-processed excipients of various batches

Parameters	Batch A	Batch B	Batch C	Batch D
Bulk Density (g/cm^3)	0.513±0	0.439±0.04	0.432±1.74	0.487±1.74
Tapped Density (g/cm^3)	0.624±0.03	0.559±0.03	0.624±1.08	0.566±1.08
Carr's Index (%)	17.79	21.47	30.77	13.96
Hausner Ratio	1.22	1.27	1.44	1.16
Angle of Repose (º)	27.4±0.12	27.1±0.2	28.7±0.06	26.7±0

3.2 Physical Properties of Excipients

The physical properties of the excipients are shown in Tables 3 and 4. Hausner ratio was used to access the flow properties of the excipients. Hausner ratio of less than 1.25 is indicative of good flowability while values of 1.5 and above suggest poor flow properties. [10] and [12]. From the result above, potato starch showed poor flowing properties, acacia gum gave a better flow property of 1.39 while that of potato starch was 1.52 which indicated poor flowability. The co-processed excipients containing acacia gum and potato starch Batches A to D gave Hausner ratios of 1.22, 1.27, 1.44 and 1.16 respectively. Batch D reflected the lowest value of 1.16, hence it is considered as the best batch which could be used in the production of directly compressible tablets. The physical admixture of Batch D (1.25: 48.75) was found to possess Hausner ratio of 1.33. Avicel CE 15, avicel HFE-102 NF, cellactose 80 which are (1.49, 1.39 and 1.26) respectively. The batches of the co-processed excipients compared well with avicel CE 15, avicel HFE-102 NF, cellactose 80.

Carr's index is an indication of the compressibility of a powder. As a general rule, powders with Carr's index of above 23 % means the powder possesses poor flow and therefore will require the use of a glidants to improve its flowability. Powders with Carr's index below 5-15 % has excellent flowability. From the results above, acacia gum was found to possess a poor flowability with Carr's index of 27.90 %, also potato starch which gave Carr's index of 34.11 % and which also means poor flow of powder. It was found that avicel CE 15 and avicel HFE-102 NF gave poor flowability with Carr's index of 32.66 % and 28.09 % except cellactose 80 which was within the range with Carr's index of 20.4 %. The physical admixture of the best batch (1.25: 48.75) gave Carr's index of 25.07 % while Batches A to D possessed 17.79, 21.47, 30.77, 13.96 % Carr's index respectively with batch D having the best Carr's index of 13.96 %.

Angle of repose is used to assess the flow properties of excipients. The angle of repose gives an indication of the inter-particulate frictional forces operating within the powder system by quantifying the resistance of the powder mass to flow. Values less than 25º is indicative of fair to good powder flow, while values greater than about 50º suggests that the material has extremely poor flow. From the results above, both potato starch and acacia gum gave a value 44.4º and 41.5 º respectively meaning they can both be satisfactorily passable for manufacturing of tablets, this could be due to the particle size or shape and their flowability can be improved by making the powders into granules so as to increase their particle sizes and consequently improve their flowability. The co-processed excipient with the ratio of (1.25: 48.75) Batch D reflected the best flow and passed with a value of 26.7º compared to the Batches A to C with the ratio of (0.5: 49.5) Batch A, (0.75: 49.25) Batch B, (1: 49) Batch C, and Physical admixture (1.25: 48.5) which had 27.4, 27.10, 28.7 and 39.6º respectively. Angle of repose for Cellactose®80, avicel CE 15, and avicel HFE-102 NF was 36.1, 47.3, and 41.0º respectively which may be due to the fact that these co-processed excipients possessed smaller particle size as shown in Table 2.

The bulk and tapped density of a material describes its packing behavior during tableting [13]. An increase in the tapped density is an advantage in tableting because the fill volume of the die would be reduced. The ranking of the tapped density for the co-processed excipients are as follows; avicel CE 15 > Batch C= Batch A > Batch D > Batch B > Cellactose®80 > avicel > HFE-102 NF respectively. This implies that the co-processed excipients showed good flowability and complete filling of the die; as a result uniformity of weight and content of compressed tablets would be achieved when employed in tableting.

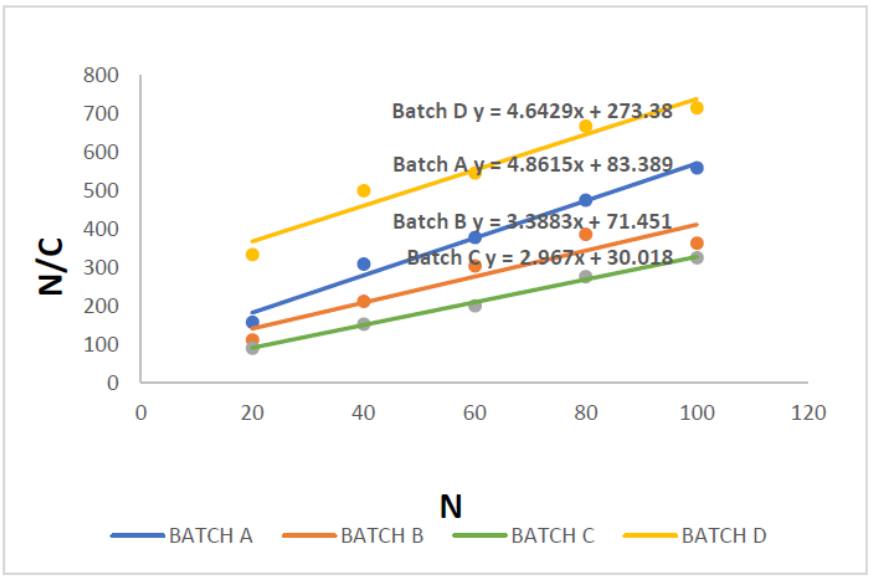

Figure 1: Plot N/C against numbers of taps for measurement of packing and cohesive properties of co-processed excipients (Batches A-D)

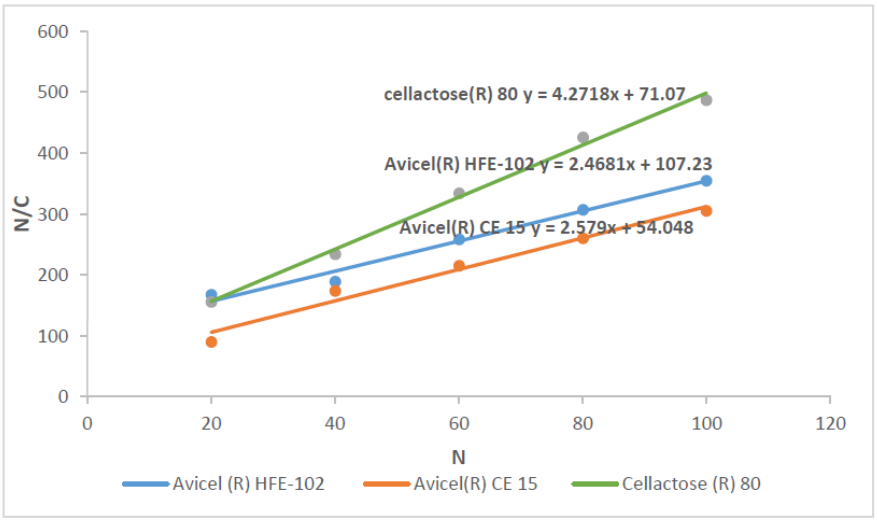

Figure 2: Plot N/C against numbers of taps for measurement of packing and cohesive properties of Avicel (R) HFE 102, Avicel (R) CE 15, cellactose 80

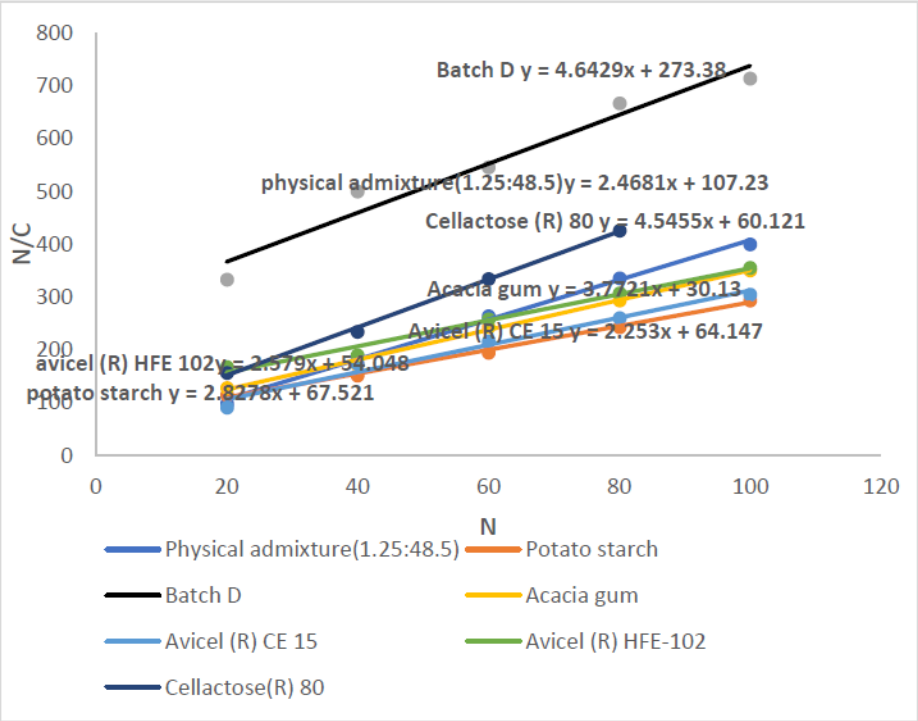

Figure 3: Plot N/C against numbers of taps for measurement of packing and cohesive properties of potato starch, avicel (R) CE 15, avicel (R) HFE 102, cellactose (R) 80, physical admixture1.25:48.5) and Batch D.

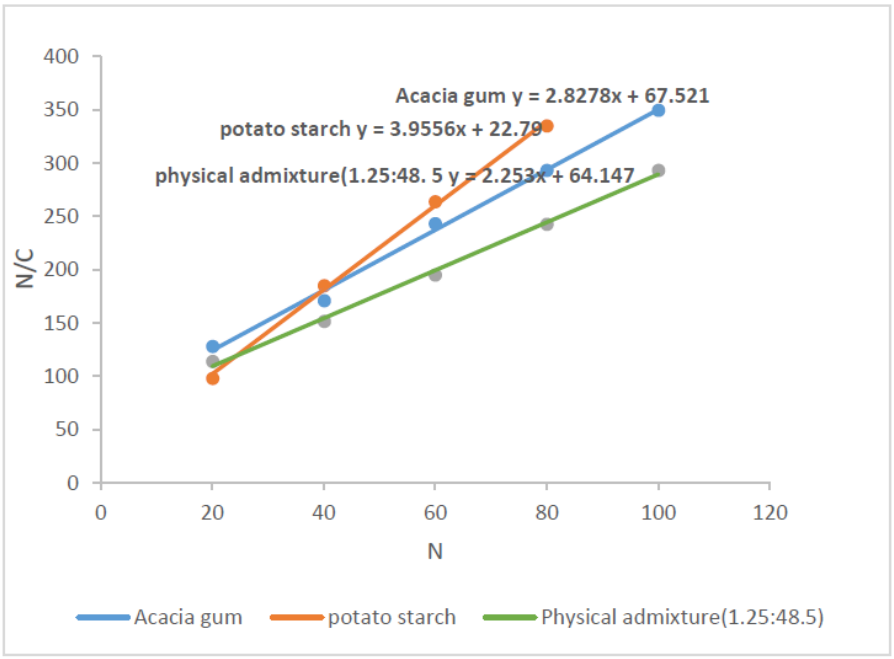

Figure 4: Plot N/C against numbers of taps for measurement of packing and cohesive properties of potato starch, acacia gum, physical admixture (1.25:48.5)

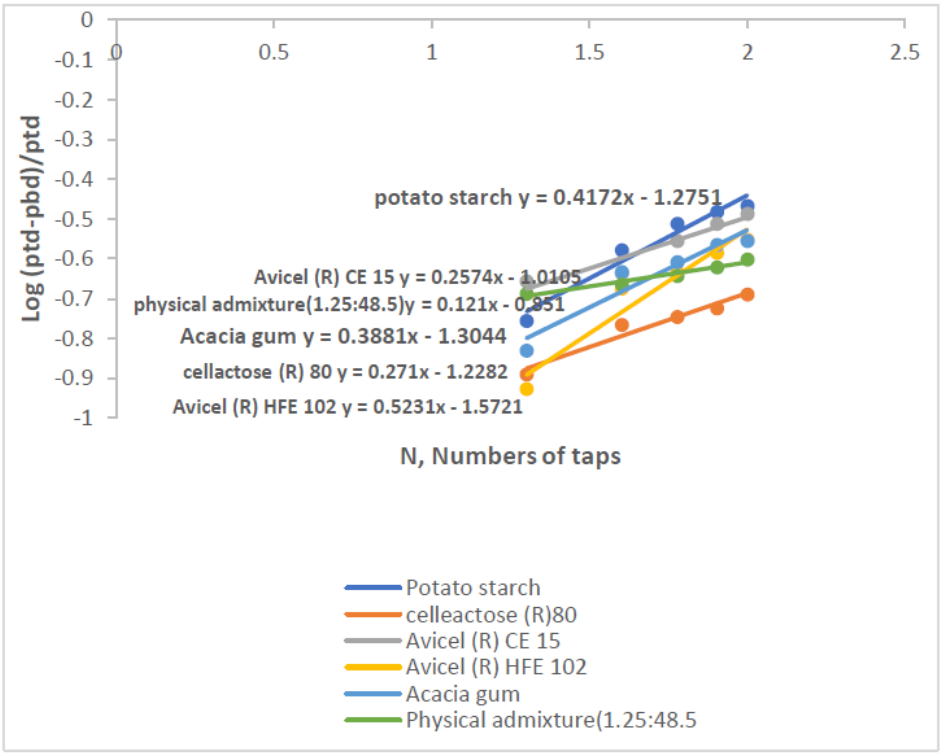

Figure 5: Plot of log (ptd-pbd)/ptd against log no of taps for potato starch, avicel (R) CE 15, avice (R) HFE 102, cellactose (R) 80, acacia gum, physical admixture (1.25:48.75)

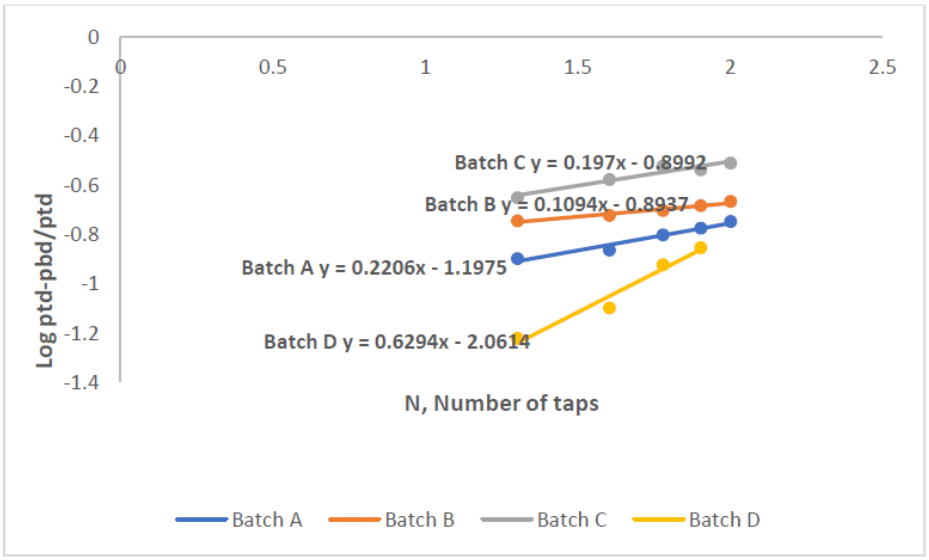

Figure 6: Plot of log (ptd-pbd)/ptd against log no of taps for co- processed excipients of batch A-D

Table 5: Packing and cohesive properties of excipients

Excipient	Maximum volume reduction 'a'	Compressibility 'b'
Acacia gum	0.35	17.20
potato starch	0.25	225.93
Co-processed excipient 0.5:49.5 A	0.21	17.18
Co-processed excipient 0.75:49.25 B	0.30	21.08
Co-processed excipient 1:49 C	0.34	10.12
Co-processed excipient 1.25:48.5 D	0.22	58.78
Physical admixture (1.25: 48.5)	0.44	28.48
Cellactose®80	0.21	15.07
avicel HFE-102 NF	0.41	43.43
avicel CE 15	0.39	20.97

The maximum volume reduction after tapping, obtained from the slope of the initial lines. A low value of 'a' indicates that the powder system has packed more densely on initial pouring into the cylinder, which implies that the powders were well packed before tapping, since tapping did not give considerate improvement in their packing

Table 6: Rate of consolidation and consolidation index

Excipient	Rate of consolidation (K)	Consolidation index (CI)
Acacia gum	0.39	-1.30
Potato starch	0.42	-1.28
Co-processed excipient 0.25:49.75 A	0.22	-1.19
Co-processed excipient 0.5:49.5 B	0.11	-0.89
Co-processed excipient 1:49 C	0.20	-0.90
Co-processed excipient 1.25:48.75 D	0.63	-2.06
Physical admixture (0.5 :49.5)	0.21	-0.85
Cellactose®80	0.27	-1.23
avicel HFE-102 NF	0.52	-1.57
avicel CE 15	0.26	-1.01

Table 7: Porosity of excipients

Excipient	Porosity	% Porosity
Acacia gum	0.927	92.7
Potato starch	0.939	93.9
Co-processed excipient 0.5:49.5 A	0.948	94.8
Co-processed excipient 0.75:49.25 B	0.961	96.1
Co-processed excipient 1:49 C,	0.934	94.3
Co-processed excipient 1.25:48.75 D	0.960	96.0
Physical admixture 1.25: 48.75 D	0.948	94.8
Cellactose®80	0.942	94.2
avicel HFE-102 NF	0.916	91.6
avicel CE 15	0.847	84.7

Porosity is the space between particles. The values depend on the amount of gum present [11]. The value of porosity for Batch D is higher than the other excipients.

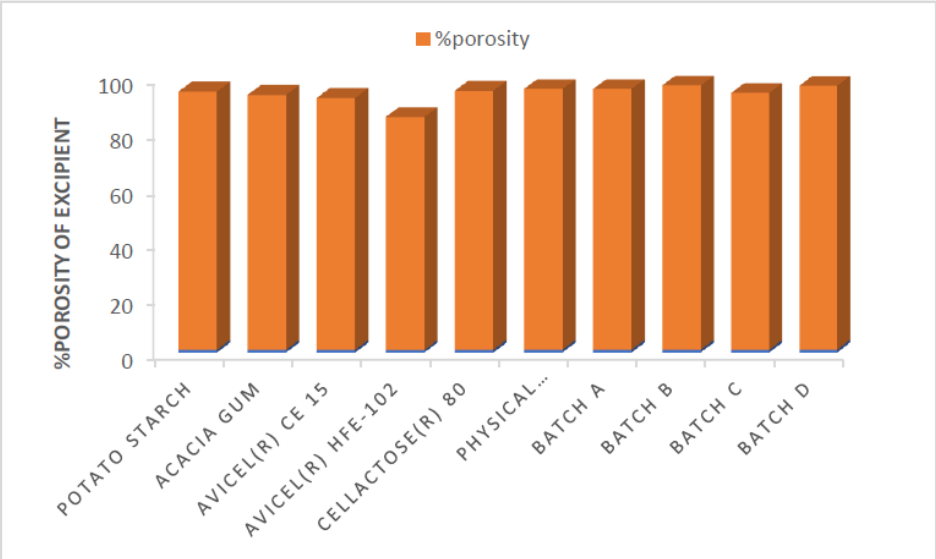

Figure 7: Percentage porosity of excipients

IV. CONCLUSION

The results of this study have shown that the co-processed excipients showed good physical properties suitable for tableting. Although the results of the co-processed excipient 1.25 (Acacia gum): 49.5 (Potato starch) was more satisfactory than other ratios due to the differences in the ratio of the acacia gum used in co-processing the potato starch powder.

Co-processing of excipients improved the flowability and physical properties of the starting materials. The use of co-processed excipients for tableting is cheaper and makes the production easier and faster because it will eliminate the use of other excipients such as disintegrants, diluents and binder.

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