IJPSR (2021), Volume 12, Issue 11 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 08 December 2020; received in revised form, 24 March 2021; accepted, 25 May 2021; published 01 November 2021

NEW CO-PROCESSED EXCIPIENTS WITH MICROCRYSTALLINE CELLULOSE AND ISOMALT BY FLUID BED. AN OPTION FOR DIRECT COMPRESSION EXCIPIENTS

A. V. Vélez Godínez [1], E. Hernández Baltazar [2], E. Amador González [3] and L.M. Melgoza Contreras [*1]

Maestría en Ciencias Farmacéuticas and Departamento de Sistemas Biológicos [1], Universidad Autónoma Metropolitana-Xochimilco, Ciudad de México, México.
Facultad de Farmacia [2], Universidad Autónoma del Estado de Morelos, México.
Facultad de Química [3], Universidad Nacional Autónoma deMéxico, Ciudad de México, México.

Keywords:

Direct compression co-processed, Isomalt, Microcrystalline cellulose, Starch 1500, Plasdone K25, Fluid bed

Correspondence to Author:
Luz María Melgoza Contreras

PhD,
Universidad Autónoma Metropolitana-Xochimilco, Departamento de Sistemas Biológicos, Calzada del Hueso1100 Colonia Villa Quietud. Alcaldía Coyoacán C.P. 04960, Ciudad de México, México.

E-mail: lmelgoza@correo.xoc.uam.mx

ABSTRACT: Objective: To elaborate and characterize new co-processed excipients for direct compression use. **Methods:** The new co-processed excipients were obtained with different proportions of microcrystalline cellulose (Avicel® PH101) and Isomalt (galenIQ® 800), using Starch® 1500 and Plasdone® K-25as binding agents in a fluid bed. Rheological characterization was performed; to determine their deformation pressure (Py), the Heckel model was applied. Tablets were elaborated with each polymer and each co-processed compound at different compaction pressures, and the behavior of the tensile strength curves was analyzed. **Results:** The range of particle size of the obtained co-processed compounds was 95.5 to 151µm. The flow velocity of the co-processed excipient elaborated with Avicel® PH101/galenIQ® 800 improved as compared to the velocity presented by the individual raw matters. **Conclusions:** The Avicel® PH101/galenIQ® 800 co-processed excipients elaborated at 60/40% and 70/30% proportions can be recommended to be used as direct compressible excipients because these proportions presented the best characteristics regarding flowability, less deformation pressure (Py) and a higher slope in the tensile strength graphs.

INTRODUCTION: In the pharmaceutical sector, there is always a strive to reduce costs derived from the constant inclusion of generic drugs in the market, which increases the level of competence, leading to the search for new alternatives (*i.e.*, obtention of co-processes); among these alternatives are to attain new formulations that will reach the cost-reducing objective without affecting the product's quality [1, 2].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.12(11).5775-84

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.12(11).5775-84

Regarding the production of oral solids, excipients are searched to allow elaborating tablets through direct compression because this manufacturing process offers diverse advantages over the wet or dry granulation process. Among them is the cost reduction; however, that process presents the disadvantage of being highly influenced by the fluidity and compressibility characteristics of the excipients [3-6]. Hence, the development of new excipients has become a niche of opportunities regarding materials innovation [7].

There are mainly three methodologies: new molecules, existing excipients with higher purity degree, or the combination of those already existing in the market; the latter is the option with the best economic and regulatory advantages [8].

Microcrystalline cellulose (MCC) is one of the excipients used in the continuous search for an ideal excipient, that is, the one to possess the required flowability and compressibility characteristics in a direct compression process [9, 10]. Since 1980, the co-processing of excipients that included the MCC with calcium carbonate [11] was introduced, and, later on, the silicified MCC was developed; in addition, sugars have been used as excipients for direct compression, like lactose (fast flow), sorbitol, mannitol, and Isomalt [12].

This work aimed at developing new multifunctional co-processed excipients with an improved flowability, excellent compressibility and an equilibrium between their deformation behavior and fracture. To achieve this, different proportions of microcrystalline cellulose (Avicel® PH101) and Isomalt (galenIQ® 800) were used with pregelatinized starch (Starch® 1500) and polyvinylpyrrolidone (Plasdone® K-25) as binding agents in a fluid bed.

MATERIALS AND METHODS:

Materials: Microcrystalline cellulose (Avicel® PH101, FMC, batch: P106817006), Isomalt (galenIQ® 800 DVA, batch: L1213924H4), polyvinylpyrrolidone (Plasdone® K-25, Ashland, batch: 1715996), pregelatinized starch (Starch® 1500, Colorcon, batch: IN525414), magnesium stearate (ADyFarm, batch: C908704), lactose (FlowLac 100, Meggle, batch: L10490), silica dioxide (HDK N20 Pharma de Wacker, batch: 60080926-C).

TABLE 1: EXPERIMENTAL DESIGN FOR THE CO-PROCESSED EXCIPIENTS

Formulation	% Avicel® PH101	% GalenIQ® 800	Binder
1	90	10	Plasdone® K25
2	80	20	
3	70	30	
4	60	40	
5	90	10	Starch® 1500
6	80	20	
7	70	30	
8	60	40	

Elaboration of Co-processed Excipients: Microcrystalline cellulose was chosen as a base excipient, and Isomalt was added at 10, 20, 30, and 40% proportions; Plasdone® K-25 and Starch® 1500 were used at a 5 and 10% w/v concentration respectively in a hydro-alcohol solution (75:25, water/ethanol), as binding agents for the granulation process, **Table 1**. The co-processed compounds were agglutinated in an *Aeromatic Fielder STREA 1* equipment, where the pressure of the equipment was 0.45 MPa and the pressure of the spraying gun was 0.1 MPa, at a drying temperature of 31 ± 2°C.

Sieving and Rheological Characterization of the Raw and Co-processed Materials: In a Retsch AS 200 sieving machine, cascade sieving was performed to know the distribution of the size of particles of used excipients and the manufactured co-processed ones; once this had been determined, we obtained the fraction with the highest population. The latter was then subjected to rheological characterization by measuring the angle of repose (Eq. 1), flow velocity (Eq. 2), Hausner index (Eq. 3), and percentage of compressibility (Eq. 4), following the method specified in the Pharmacopeia [13].

$$AR = tan^{-1}\left(\frac{h}{r}\right) \quad .....1$$

Where h is the height and r the radius

$$Vf = \frac{g}{t} \quad .....2$$

Where *g* are the grams and *t* the time in seconds

$$HI = \frac{D_t}{D_b} \quad .....3$$

Where D_b is the bulk density and D_t the tapped density

$$\%C = \frac{D_t - D_b}{D_t} \times 100 \quad .....4$$

Where D_b is the bulk density and D_t the tapped density

In 2019, Zacarías *et al.*, [14] proposed an equation involving all the previous parameters, which allows determining the flowability of the raw materials and the obtained co-processed compounds and corresponds to the equation that calculated the flow index. The equation allows establishing a relation between the parameter obtained directly, as is the V_f, and the parameters calculated indirectly, as are AR, %C, and HI (Eq.5).

$$Flow\ index = \frac{(Vf * 100)}{(AR * \%C * HI)} \quad (5)$$

The greater the V_f, the better will be the flowability of the material; hence, it was considered directly proportional in the flow index equation; whereas for AR, %C, and HI, the smaller their value, the flowability of the powder will be better; hence, they were considered indirectly proportional to the flow index in the equation.

The Heckel Model: For this test, three tablets were elaborated with each co-processed compound and three tablets with each individual raw material in a hydraulic press (Carver, mod 3912) at eight different pressures (35.5, 70.2, 105.6, 141, 176.5, 211.8, 247.1, 282.3 MPa, during 5 sec), using 13-mm-diameter punches, weighing 500 mg. Measurements of tablets were performed 24 h after their elaboration, and their relative density was determined with Eq. 6. [15]

$$\rho_{relative} = \frac{\rho_b}{\rho_t} \quad \text{.....6}$$

Where P_b is the bulk density of the tablets and P_t is the true density of the powder.

Data were plotted according to Heckel's model, with Eq. 7; the least square method was used to determine the equation of the straight line.

$$ln\frac{1}{1-\rho_{relative}} = kP + A \quad \text{.....7}$$

Where *k* is the slope of the obtained straight line, P is the applied pressure (axis *x*), and A is the intercept in axis *y*.

To determine the deformation pressure (Py), the inverse of the slope was calculated (Eq. 8).

$$Py = \frac{1}{K} \quad \text{.....8}$$

Tensile Strength: The resistance to diametral rupture of previously mentioned tablets was determined in a hardness meter (Pharma Alliance Group PAH-01), and these results were used to perform the tensile strength curves as a function of the compaction force. The tensile strength (σ_T) was assessed according to Eq. 9.

$$\sigma_T = \frac{2F}{\pi * d * h} \quad \text{.....9}$$

Where *F* represents the resistance to rupture, *d* is the diameter of the tablet, and *h* is the height or thickness.

Micrographs: Avicel® PH101 and galenIQ® 800 were observed in a digital microscope (DinoLite AM4515ZT), as well as the co-processed compounds obtained with them aiming at observing the possible changes after the binding process.

Statistical Analysis: A *post hoc* (Tukey) test was used to compare the average particle sizes of the co-processed compounds obtained with both binders at each of the used proportions. To compare the rheological characterization parameters, as well as the Py values and the slopes of the tensile strength graphs, subjected to different compaction pressures, a one-way variance analysis (ANOVA) was used, followed by a Tukey test with the SPSS software.

RESULTS AND DISCUSSION:

Sieving and Rheological Characterization: The size of the average particle for Avicel® PH101 was 69µm and 40 µm for galenIQ® 800, and those obtained for the co-processed compounds are summarized on **Table 2**.

TABLE 2: PARTICLE SIZE OF CO-PROCESSED FROM AVICEL® PH101/ GALENIQ® 800, BINDING WITH PLASDONE® K25 AND STARCH® 1500

Excipient ratio		Binder	
Avicel® PH101	GalenIQ® 800	Plasdone® K25 (µm)	Starch® 1500 (µm)
90	10	151.0	125.4
80	20	140.5	140.36
70	30	140.5	132.37
60	40	95.5	147.52

The *post hoc* test used to compare the average particle sizes obtained with both binders at each of the used proportions revealed a significant difference only for the co-processed compounds elaborated with the Avicel® PH101/galenIQ® 800 (60/40%) proportion; whereas for the other proportions it was indistinct using different binders regarding the average particle sizes to be obtained.

Table 3 and **4** depict the results of the rheological tests performed on the co-processed compounds made with Avicel® PH101 and galenIQ® 800, as well as the flowability that they possess according to the classification provided by Pharmacopeia [13].

TABLE 3: RHEOLOGIC CHARACTERISTICS OF CO-PROCESSED AVICEL® PH101/GALENIQ® 800, BINDER PLASDONE® K25

	Avicel® PH 101	GalenIQ® 800	F1	F2	F3	F4
Angle of Repose	32.90	57.51	36.17	33.64	32.86	31.26
Flow character	Good	Poor	Fair	Good	Good	Good
Compresibility index (%C)	20	22	22	23	23	22
Hausner ratio (HR)	1.25	1.28	1.28	1.30	1.30	1.28
Flow HR/%C	Fair	Passable	Passable	Passable	Passable	Passable
Flow rate (g/s)	2.50	1.22	1.62	1.71	1.69	2.81
Flow index	0.30	0.08	0.16	0.17	0.17	0.32

TABLE 4: RHEOLOGIC CHARACTERISTICS OF CO-PROCESSED AVICEL® PH101/GALENIQ® 800, BINDER STARCH® 1500

	Avicel® PH 101	GalenIQ® 800	F5	F6	F7	F8
Angle of Repose	32.90	57.51	28.66	28.59	28.74	28.23
Flow character	Good	Poor	Excellent	Excellent	Excellent	Excellent
Compresibility index (%C)	20	22	20	20	20	19
Hausner ratio (HR)	1.25	1.28	1.25	1.25	1.25	1.23
Flow HR/%C	Fair	Passable	Fair	Fair	Fair	Fair
Flow rate (g/s)	2.50	1.22	2.45	2.91	7.95	3.50
Flow index	0.30	0.08	0.34	0.41	1.11	0.53

Co-processed compounds Avicel® PH101/ galenIQ® 800with Plasdone® K25: The ANOVA test used to assess the presence of significant differences among AR values, as well as %C and HI of the co-processed compounds made with Avicel® PH101 and galenIQ® 800, elaborated with Plasdone® K25 revealed that there are no statistically significant difference among the co-processed compounds for these parameters.

When applying the same test for the V_f, a statistically significant difference was found among groups **Table 5**, the test was followed by the Tukey test **Table 6**, revealing that the Avicel® PH101/ galenIQ® 800 (60/40%) proportion presented a significant difference with respect to the other proportions; *i.e.*, the flow velocity was significantly higher than that of the other co-processed excipients.

TABLE 5: ONE WAY ANALYSIS OF VARIANCE OF FLOW RATE OF CO-PROCESSED AVICEL® PH101 AND GALENIQ®800, BINDING WITH PLASDONE® K25

ANOVA					
Flow rate	**Sum of squares**	**Df**	**Mean square**	**F-ratio**	**Sig.**
Between groups	79.260	7	11.323	143.878	0.000
Within groups	1.259	16	0.79		
Total	80.519	23			

TABLE 6: TUKEY TEST APPLIED TO THE AVERAGE OF FLOW RATE OF CO-PROCESSED WITH AVICEL® PH101 AND GALENIQ®800, BINDING WITH PLASDONE® K25

Multiple comparisons						
Variable: Flow rate					95% Confidence interval	
HSD Tukey						
(I) Ratio	**(J) Ratio**	**Difference of means (I-J)**	**Standard error of the difference**	**Sig.**	**Lower limit**	**Upper limit**
60/40	70/30	1.1217*	0.1019	0.000	0.7954	1.4480
	80/20	1.0983*	0.1019	0.000	0.7720	1.4247
	90/10	1.1259*	0.1019	0.000	0.7996	1.4522
70/30	60/40	-1.1217*	0.1019	0.000	-1.4480	-0.7954
	80/20	-0.2337	0.1019	0.995	-0.3497	0.3029
	90/10	0.0042	0.1019	1.000	-0.3221	0.3305
80/20	60/40	-1.0983*	0.1019	0.000	-1.4247	-0.7720
	70/30	0.2337	0.1019	0.995	-0.3029	0.3497
	90/10	0.2753	0.1019	0.993	-0.2988	0.3538
90/10	60/40	-1.1259*	0.1019	0.000	-0.2988	-0.7996
	70/30	-0.0042	0.1019	1.000	-1.4522	0.3221
	80/20	0.2753	0.1019	0.993	-0.3538	0.2988

*Difference of means is significant at level 0.05

Co-processed compounds Avicel® PH101/ galenIQ® 800 with Starch® 1500: The ANOVA test revealed that there was no statistically significant difference among groups regarding the AR, bulk and tapped density tests, nor for the % C or the HI.

For V_f parameter, differences existed among groups, revealing that the proportion with a significantly higher flow velocity (7.95g/s) was that of Avicel® PH101/galenIQ®800 (70/30%), **Table 7**.

TABLE 7: TUKEY TEST APPLIED AT AVERAGE OF FLOW RATE OF CO-PROCESSED WITH AVICEL® PH101 AND GALENIQ®800, BIDING WITH STARCH® 1500

Multiple comparisons						
Variable: Flow rate					95% Confidence interval	
HSD Tukey						
(I) Ratio	(J) Ratio	Difference of means (I-J)	Standard error of the difference	Sig.	Lower limit	Upper limit
60/40	70/30	-4.2526	0.3075	0.000	0.7954	1.4480
	80/20	0.4543	0.3075	0.492	0.7720	1.4247
	90/10	0.8975	0.3075	0.075	0.7996	1.4522
70/30	60/40	4.2526*	0.3075	0.000	3.2679	5.2373
	80/20	4.7069*	0.3075	0.000	3.7222	5.6916
	90/10	5.1501*	0.3075	0.000	4.1654	6.1347
80/20	60/40	-0.4543	0.3075	0.492	-1.4390	0.5304
	70/30	-4.7069*	0.3075	0.000	-5.6916	-3.7222
	90/10	0.4432	0.3075	0.511	-0.5415	1.42786
90/10	60/40	-0.8875	0.3075	0.075	-1.8821	0.8722
	70/30	-5.1501*	0.3075	0.000	-6.1347	-4.1654
	80/20	-0.4432	0.3075	0.511	-1.4279	0.5415

*Difference of means is significant at level 0.05

It is important to point out that when using Starch® 1500, the flowability according to AR was excellent, in contrast with those elaborated with Plasdone K25, which were just good and adequate; this is due to the excellent sliding properties of starch, which is also a good binder.

Flowability and compressibility are among the main characteristics that a good excipient must have for direct compression [12, 16]. The parameters considered in the flowability of the co-processed compounds were the AR, %C, HI, and V_f **Table 3** and **4**; therefore, Avicel® PH101/galenIQ®800 (60/40%) co-processed compound with Plasdone K25 can be considered the best for those and Avicel® PH101/galenIQ®80 (70/30%) with Starch® 1500.

Evaluation of Compressibility and Resistance to Fracture of Obtained Co-processed Compounds:

Heckel Model: This model assesses the effect of the pressure applied on the relative density of a powder during compression. When applying the Heckel equation (Eq. 7), a straight line is obtained, where the inverse of the slope (*Py*) will indicate the minimal pressure required to achieve the plastic deformation of the material being studied.

The adjustment of the behavior of the different co-processed compounds to the model is depicted in **Fig. 1** and **2**, in which the linear relation between 75 and 225 MPa was considered.

Fig. 1 depicts the compressibility profiles of the co-processed compounds elaborated with Plasdone K25, which did not reveal a large variability.

Polyvinylpyrrolidone (PVP) acts as a plasticizer in granulated systems due to it glass transition temperature (T_g), leading the granulated product to go from a glass state to a flexible one, presenting better compression and compaction properties,[17] although in this combination of materials its effect was not significant.

Fig. 2, where Starch 1500 was used as a binder, reveals that as the proportion of galenIQ® 800 increased, the slope was modified, particularly in the 60/40 proportion, which was much better than the other co-processed compounds, even better than Avicel® PH101.

Hence, the pressure required to obtain a stable tablet is low (*Py*), presenting a better compressibility **Table 8**.

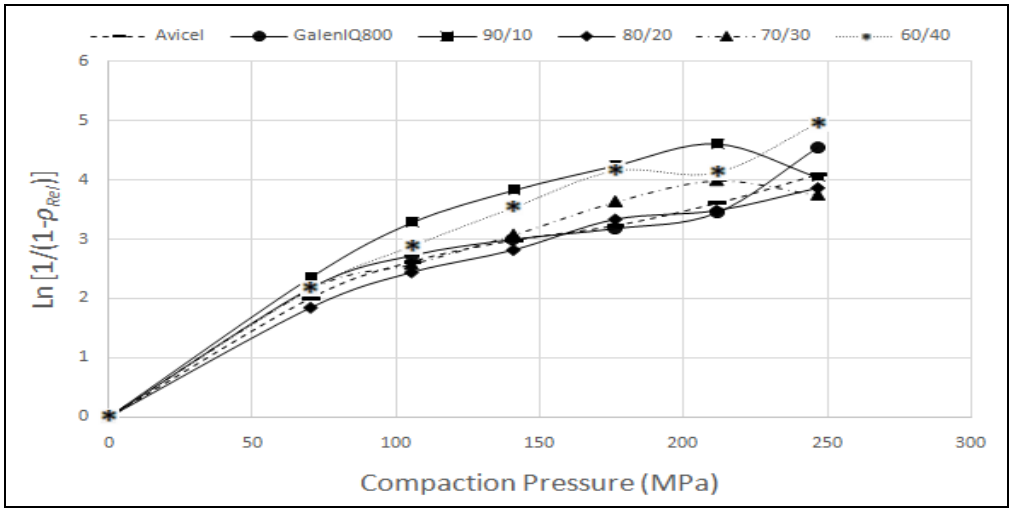

FIG. 1: HECKELGRAPHS FOR AVICEL® PH101/GALENIQ® 800 COPROCESSED, PLASDONE® K25 AS BINDER

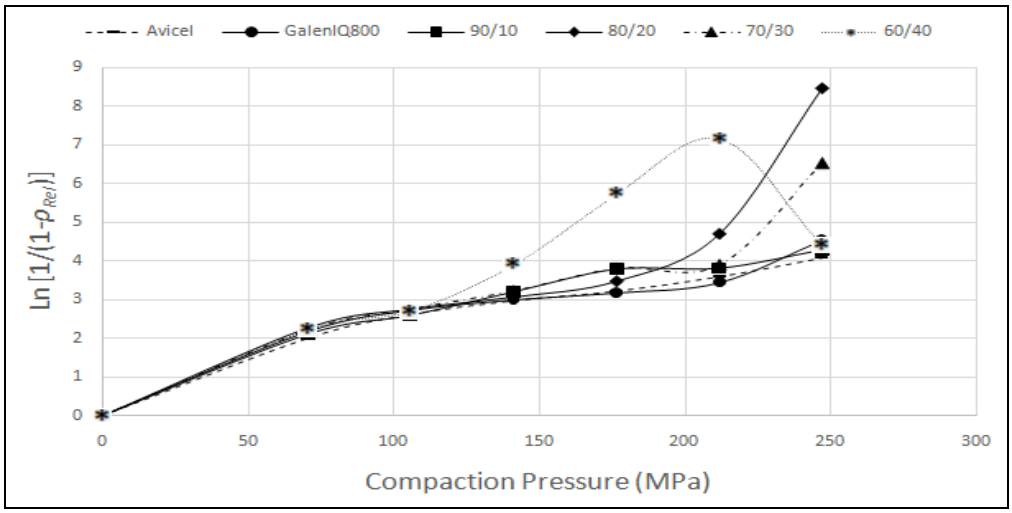

FIG. 2: HECKELGRAPHS FOR AVICEL® PH101/GALENIQ® 800 CO-PROCESSED, STARCH® 1500 AS BINDER

The obtained *Py* values, calculated for co-processed compounds, are shown in **Table 8**, considering that the greater the value of *Py*, the greater compaction pressure will be needed to alter the particles and obtain a consolidated tablet [18-19].

TABLE 8: DEFORMATION PRESSURE (Py) VALUES FOR CO-PROCESSED WITH AVICEL® PH101/GALENIQ® 800

Raw	Materials	Co-processed using Plasdone® K25 as binder			
Avicel® PH101	GalenIQ® 800	F1	F2	F3	F4
93.26	117.06	64.07	84.29	74.46	67.56
Raw	**materials**	**Co-processed using Starch® 1500 as binder**			
Avicel® PH101	GalenIQ® 800	F5	F6	F7	F8
93.26	117.06	76.81	62.63	79.92	27.54

By means of ANOVA, no statistically significant difference was found in the values of *Py* for the co-processed compounds elaborated with Plasdone® K25 **Table 8**; however, it is important to observe that the co-processed compound with the 60/40 relation presented the lowest *Py* values, just like the 90/10 relation.

In the Starch® 1500 bound co-processed compounds, there was a statistically significant difference in the 60/40 relation, which presented a 3-times lower value of *Py* with the Avicel® PH101, which is an excellent behavior.

On the other hand, determining the tensile strength of the tablets as a function of the compaction force per square centimeter and performing the corresponding graphs allowed calculating the values of the slopes, which were indicative of the compressibility presented by the powders **Table 9**.

TABLE 9: SLOPE FROM GRAPHS OF TENSILE STRENGTH

Raw materials		Co-processed using Plasdone® K25 as binder			
Avicel® PH101	**GalenIQ® 800**	**F1**	**F2**	**F3**	**F4**
0.37	0.12	1.23	0.70	0.83	0.59
		Co-processed using Starch® 1500 as binder			
Avicel® PH101	**GalenIQ® 800**	**F5**	**F6**	**F7**	**F8**
0.37	0.12	0.50	0.58	0.75	0.54

By means of ANOVA analysis of the slopes, a statistically significant difference was determined among groups, followed by a Tukey test, observing that all groups are different among themselves. The values of these slopes indicate the compressibility that the powder will show in a compression process; a greater slope will represent better compressibility. That is, with a lower compression force, tablets with a greater mechanical resistance will be obtained. This characteristic can be observed in the co-processed compound made with a 70/30% proportion of Avicel® PH101/galenIQ® 800 with Starch® 1500. Regarding those compounds made with Plasdone® K25, a greater slope was obtained with the 90/10% proportion of Avicel® PH101/galenIQ® 800. It is important to mention that this was not considered because tablets with a very high hardness were obtained outside of the range of the hardness meter used; thus, only two points were obtained, and the slope was invalidated. Therefore, the co-processed compound with the highest slope was that of the 70/30% Avicel® PH101/galenIQ® 800 relations **Fig. 3** and **4**.

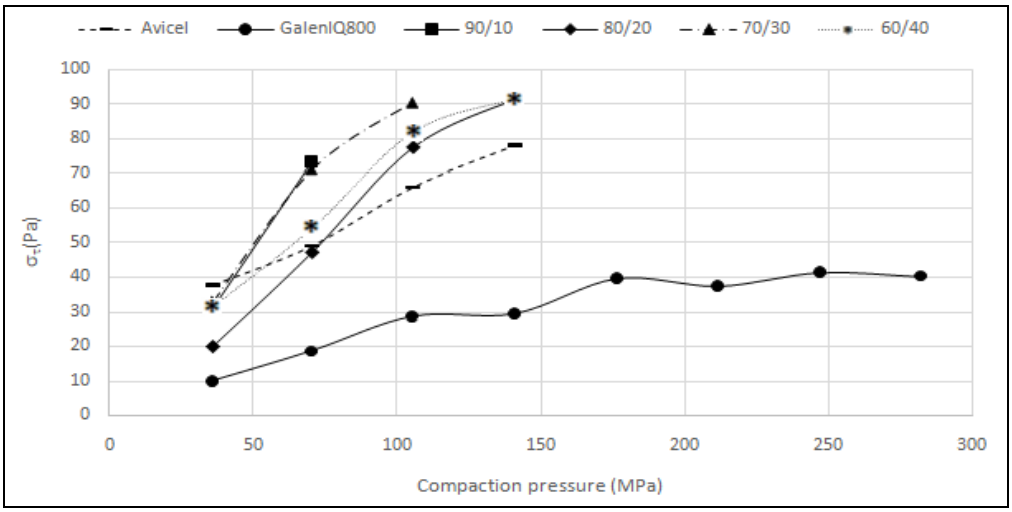

FIG. 3: TENSILE STRENGTH GRAPHS, FOR AVICEL® PH101/GALENIQ® 800 CO-PROCESSED, PLASDONE® K25 AS BINDER

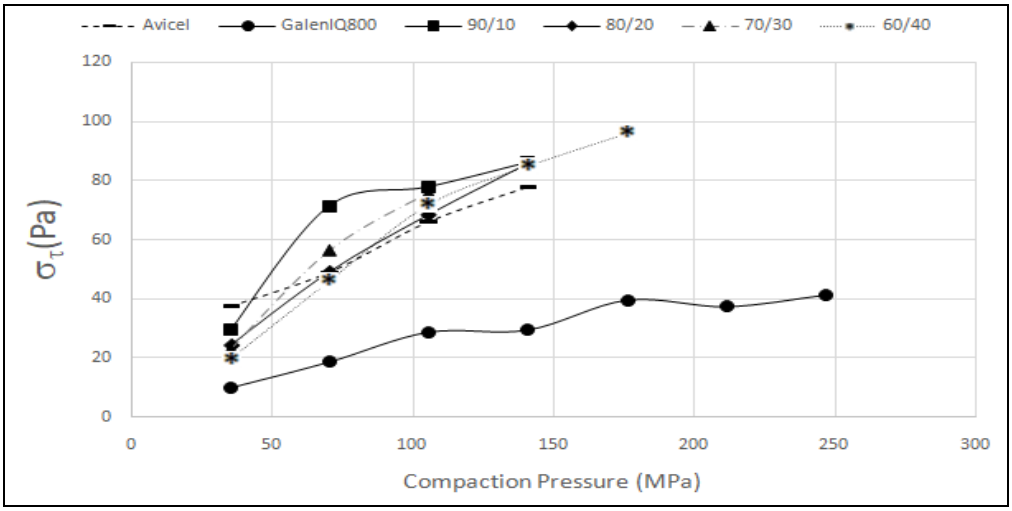

FIG. 4: TENSILE STRENGTH GRAPHS, FOR AVICEL® PH101/GALENIQ® 800, CO-PROCESSED, STARCH® 1500 AS BINDER

Table 10 summarizes the best co-processed compounds according to the evaluated properties.

TABLE 10: RELEVANT PROPERTIES OF CO-PROCESSED EXCIPIENTS WITH DIFFERENT BINDER

	Plasdone® K25	Starch® 1500
Angle of repose	Good (3 CP) Fair (1 CP 90/10%)	Excellent (4 CP)
% Compressibility and Hausner index	Acceptable (4 CP)	Acceptable (4 CP)
Flow rate	Avicel® PH101/GalenIQ®800 60/40%	Avicel® PH101/GalenIQ®800 70/30%
Deformation pressure (Py)	Avicel® PH101/GalenIQ®800 60/40%	Avicel® PH101/GalenIQ®800 60/40%
Slopes Tensile strength *vs* Pressure	Avicel® PH101/GalenIQ®800 70/30%	Avicel® PH101/GalenIQ®800 70/30%
Flow index	Avicel® PH101/GalenIQ®800 60/40%	Avicel® PH101/GalenIQ®800 70/30%

CP: Co-processed

Microphotographs: The microphotographs of **Fig. 5** show the raw materials used for the elaboration of the co-processed compounds; it can be observed that galenIQ®800 presents a rounded shape, but with irregular borders **Fig. 5a**, whereas the microcrystalline cellulose has an elongated shape **Fig. 5b**, like a needle.

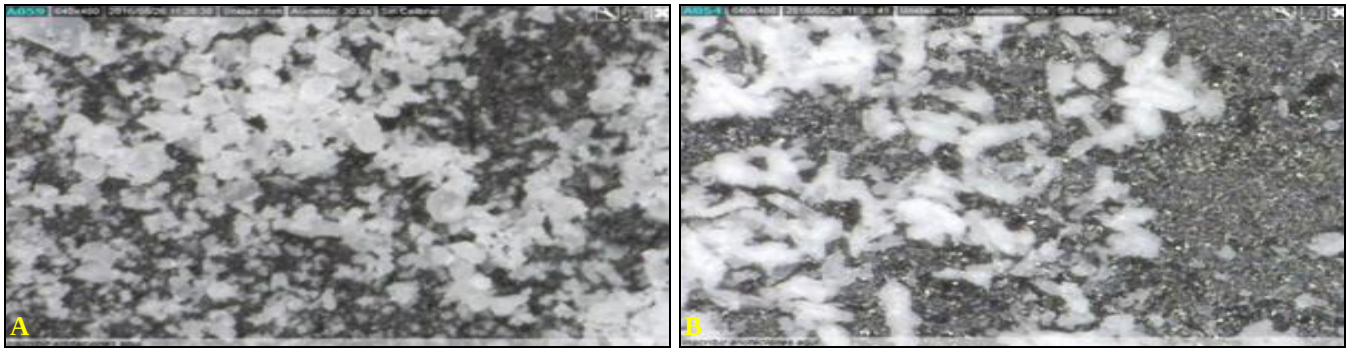

FIG. 5: PHOTOGRAPHS OF RAW MATERIALS AT 30X: A) GALENIQ® 800 AND B) AVICEL® PH101

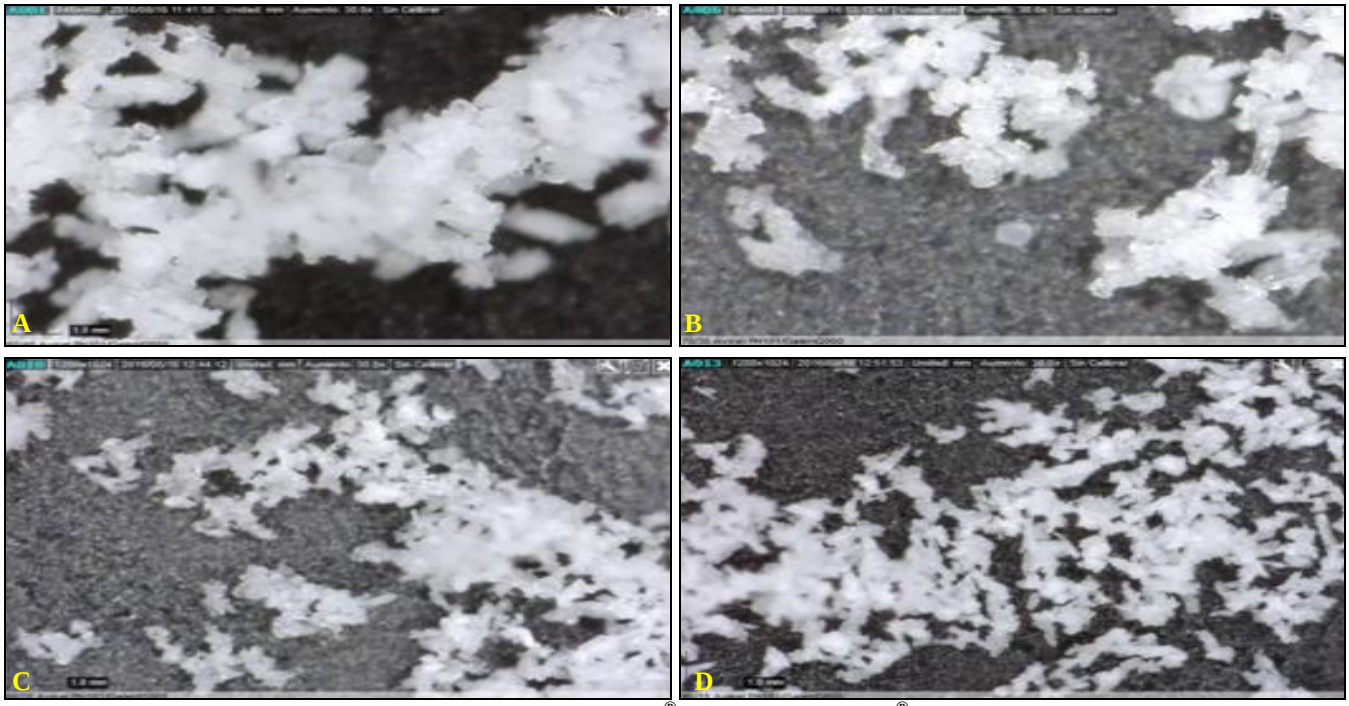

FIG. 6: PHOTOGRAPHS OF CO-PROCESSED AVICEL® PH101/GALENIQ® 800 A 30X: A) 60/40%, B) 70/30%, C) 80/20% Y D) 90/10%. BINDING WITH 5% W/V DE PLASDONE® K25

Fig. 6 shows the microphotographs of the co-processed compounds made with a binding solution at 5% of Plasdone® K25, where binding of the components can be seen **Fig. 6a-6d**. **Fig. 6c** and **6d** clearly show that the lower the amount of galenIQ® 800 in the co-processed compound, the needle-shaped microcrystalline cellulose particles predominate.

The microphotographs of **Fig. 7** show the co-processed compounds made with Starch 1500, revealing agglomeration of the components, which can be seen among the Avicel® PH101 particles (needle-shaped particles). In the microphotographs of those co-processed compounds in which the proportion of galenIQ® 800 was increased, an agglomeration of Avicel® PH101 particles was observed. No clear differentiation was observed in the particles between the components because the galenIQ® 800 was partially solubilized in the solvent used in the wet granulation process, achieving with this a joint agglomeration.

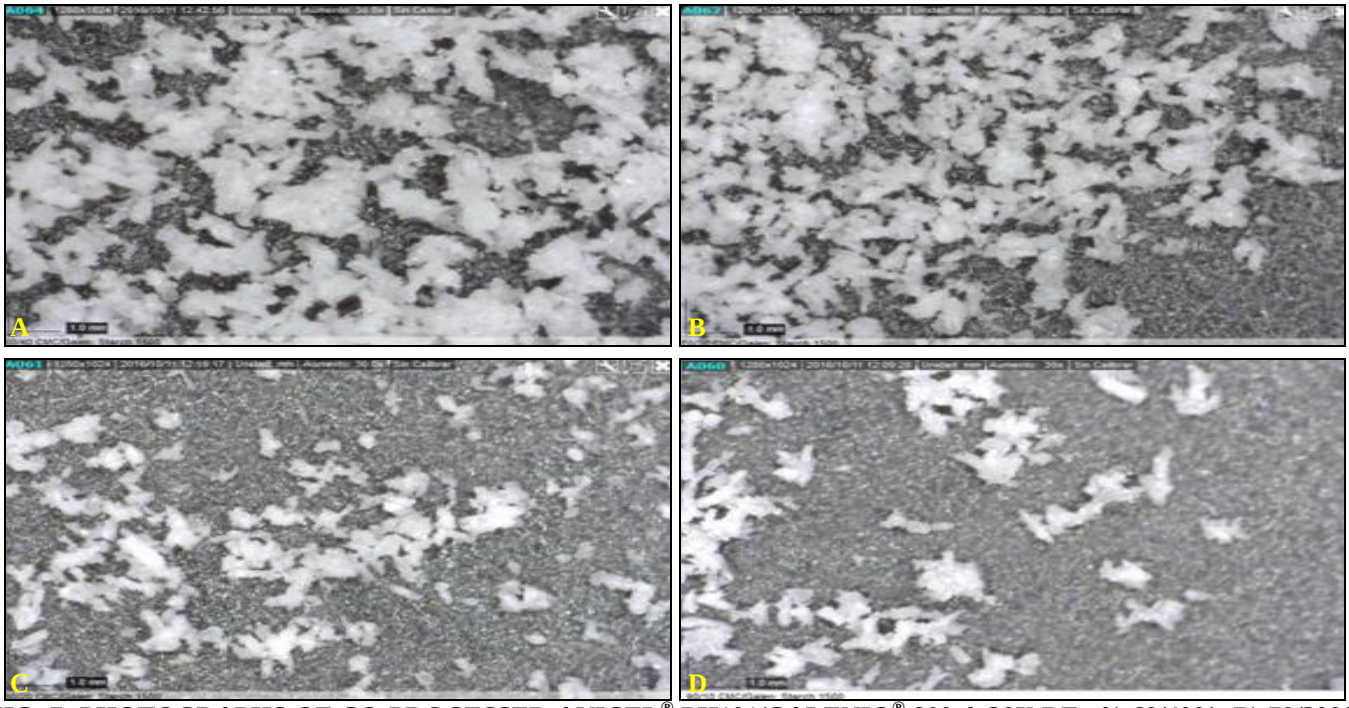

FIG. 7: PHOTOGRAPHS OF CO-PROCESSED AVICEL® PH101/GALENIQ® 800 A 30X DE: A) 60/40%, B) 70/30%, C) 80/20% AND D) 90/10%. BINDING WITH 10% W/V STARCH® 1500

CONCLUSION:

- The new Avicel® PH101/galenIQ® 800 (60/40%) co-processed excipient with Plasdone® K25 presented a better flow than raw materials (10%).
- The new Avicel® PH101/galenIQ® 800 (70/30%) co-processed excipient with Starch® 1500 have a 320% better flow; Avicel® PH101/galenIQ® 800 (60/40%) presented a 40% better flow than the raw materials.
- The equation for the new flow index allows calculating the flowability of the materials incorporating more parameters than the traditional determinations; in addition, it presents a better differentiation of the behavior of the materials than the traditional tests of the Hausner index % Compressi-bility, or angle of repose.
- Pressure for the plastic deformation of the new Avicel® PH101/galenIQ®800 (60/40%) co-processed compound with Starch® 1500 was 300% lower than the plastic deformation pressure of Avicel® PH101, which is an excellent result.
- Compressibility ofAvicel® PH101/galenIQ® 800 (70/30%) with Plasdone® K25 was 224% better than that of Avicel® PH101 and compressibility of this co-processed with

Starch® 1500 was 202% better than that of Avicel® PH101.

- Thus, new Avicel® PH101/GalenIQ® 800 co-processed compounds at a 60/40 and 70/30% proportion, elaborated with Plasdone® K25 or Starch® 1500, can be recommended for their commercialization as excipients for direct compression because they present improved characteristics of flowability and compressibility with respect toAvicel® PH101 or galenIQ® 800.

- To elaborate on these new co-processed compounds, Starch® 1500 was the best binder because it influenced better the performance (flowability, deformation pressure, and compressibility) than Plasdone® K25.

ACKNOWLEDGEMENT: Ana Vanessa Vélez Godínez thanks CONACyT for the fellowship to perform the MS studies in Pharmaceutics (fellowship No. 408872).

CONFLICTS OF INTEREST: The authors declare that they have no conflicts of interest.

REFERENCES:

1. Lekshmi P, Pramod K and Ajithkumar K: Co-processed excipients for tabletting. Research Journal of Pharmaceutical Dosage Forms and Technology 2016; 8(1): 46-54.
2. Benabbas R, Sanchez-Ballester NM, Bataille B, Sharkawi T and Soulairol I: Development and pharmaceutical performance of a novel co-processed excipient of alginic acid and microcrystalline cellulose. Powder Technology 2021; 378: 576-84.
3. Eraga S, Arhewoh M, Uhumwangho M and Iwuagwu M: Characterisation of a novel, multifunctional, co-processed excipient and its effect on release profile of paracetamol from tablets prepared by direct compression. Asian Pacific Journal of Tropical Biomedicine 2015; 5(9): 768-72.
4. Sun C and Kleinebudde P: Mini review: Mechanisms to the loss of tablet ability by dry granulation. European Journal of Pharmaceutics and Biopharmaceutics 2016; 106: 9-14.
5. Salah A: Study of the tableting properties of MCR, a newly co-processed cellulose-based direct compression excipient. Turkish Journal of Pharmaceutical Sciences 2019; 16(2): 161-68.
6. Franc A, Vetchý D, Vodáčková P, Kubaľák R, Jendryková L and Goněc R: Co-processed excipients for direct compression of tablets. Ceská Slovenska Farmacie 2018; 67: 175-81.
7. Chowdary K and Ramya K: Recent research on co-processed excipients for direct compression-a review. International Journal of Comprehensive Pharmacy 2013; 2(1): 1-5.
8. Marwaha M, Sandhu D and Marwaha R: Coprocessing of excipients: a review on excipient development for improved tabletting performance. International Journal of Applied Pharmaceutics 2010; 2(3): 41-47.
9. Vodacková P, Vraníková B, Svacinová P, Franc A, Elbl J, Muselík J, Kubalák R and Solný T: Evaluation and comparison of three types of spray dried coprocessed excipient Avicel for direct compression. Bio Med Research International 2018; 1-15. doi.org/10.1155/ 2018/2739428
10. Thoorens G, Krier F, Rozet E, Carlin B and Evrard B: Understanding the impact of microcrystalline cellulose physicochemical properties on tabletability. International Journal of Pharmaceutics 2015; 490(1-2): 47-54.
11. SujathaKumari M, Prasanthi C, SudhaBhargavi C, PraveenaKumari M and Ushasri S: Reassessment of novel co-processed multifunctional excipients. International Research Journal of Pharmaceutical and Applied Sciences 2013; 3(4): 122-28.
12. Nachaegari S and Bansal A: Coprocessed excipients for solid dosage forms. Pharm Technol 2004; 42: 52-64.
13. Farmacopea de los Estados Unidos Mexicanos, 2019; 12ª edición, Vol. I Secretaría de Salud, México.
14. Zacarías U, Vélez AV, Amador E, Hernández E, Sánchez Z and Melgoza LM: Evaluación reológica del coprocesado Avicel®PH 101/GalenIQTM 800 y su desempeño en la elaboración de tabletas de paracetamol.Revista Mexicana de Ciencias Farmacéuticas 2020, 47(4): 104-10.
15. Ilkka J and Paronen P: Prediction of the compression behaviour of powder mixtures by the Heckel equation. International J of Pharmaceutics 1993; 94(1-3): 181-87.
16. Rakesh P and Bhavsar M: Directly compressible materials via co-processing. International Journal of Pharmaceutical Technology Research 2009; 1(3): 745-53.
17. Oksanen CA and Zografi G: The relationship between the glass transition temperature and water vapor absorption by poly(vinylpyrrolidone). Pharmaceutical Research: An Official Journal of the American Association of Pharmaceutical Scientists 1990; 7: 654-57.
18. Mahmoodi F, Klevan I, Nordström J, Alderborn G and Frenning G: A comparison between two powder compaction parameters of plasticity: The effective medium a parameter and the Heckel 1/K parameter.International Journal of Pharmaceutics 2013; 453(2): 2295-299.
19. Castañeda O, Caraballo I, Bernad MJ and Melgoza LM: Comparison of the performance of two grades of metformin hydrochloride elaboration by means of the SeDeM system, compressibility, compactability, and process capability indices. Drug Development and Industrial Pharmacy 2021; 47(3): 484-97.

How to cite this article:
Godínez AVV, Baltazar EH, González EA and Contreras LMM: New co-processed excipients with microcrystalline cellulose and isomalt by fluid bed. an option for direct compression excipients. Int J Pharm Sci & Res 2021; 12(11): 5775-84. doi: 10.13040/IJPSR.0975-8232.12(11).5775-84.