Available online at https://asric.africa/health-sciences
ASRIC Journal on Health Sciences Vol.3(1)(2023) 77-88

A Novel Co-Processed Excipient with Enhanced Direct Compression Functionality for Improved Diluent Performance in Ibuprofen Tablets

Mohammed Blessing Boma[1*], Tijjani Sambo Fatima[1], Yahaya, Zwanden Sule[1], Mallam Danjuma[2]

[1]Department of Pharmaceutics & Industrial Pharmacy, Faculty of Pharmaceutical Sciences, Kaduna State University, Kaduna
[2]Department of Pharmacology & Toxicology, Faculty of Pharmaceutical Sciences, Kaduna State University, Kaduna

*Corresponding author: boma.mohammed@kasu.edu.ng

Received 20 July 2023; revised 09 August 2023; accepted 10 October 2023

Abstract

Recently, excipient development comprising a mixture of two or more materials assembled in a single frame by means of particle engineering, known as co-processed excipients, has gained enormous popularity. The study was undertaken to evaluate the suitability of a newly developed co-processed excipient, CPE (lactose 90%, mucin 5% and corn starch BP 5%) obtained as the optimized composition from the design of experiment (DOE) as a functional diluent in comparison with other diluents. Fourier transform infra-red (FTIR) was carried out on the single and CPE components and further evaluated for their micromeritic properties, compressed into tablets by direct compression. The produced tablets were evaluated using British Pharmacopoeia methods. The data obtained from the different evaluation parameters containing the CPE revealed good flow properties (flow rate, angle of repose, Carr's index and Hausner's ratio were 2.02g/sec, 18.43^0, 3.98% and 1.04 respectively), most of the peaks of CPE in the final spectra were consistent with lactose and the tablets compared well with the reference standards. The study has shown the potential of CPE as a directly compressible diluent in tablet formulation with enhanced functionality as well as comparing well with the available standards.

Keywords: route, co-processed excipient, ibuprofen, diluent, tablets.

Introduction

The need for novel excipients and their development is growing in part because current pharmaceutical materials are not up to par in meeting the critical functionality requirements of contemporary manufacturing equipment and/or sophisticated drug delivery systems, which results in products that do not meet target quality product profiles (QTPPs) (Kozarewicz and Loftsson, 2018).

Furthermore, the pharmaceutical industry's vision and adoption of lean manufacturing principles, which are aimed at reducing the time it takes for formulated products to reach the market, increasing production efficiency, and guaranteeing a steady and reasonably priced supply of high-quality medicines, have fundamentally altered the way pharmaceutical products are created (Sieckmann et al., 2018). When the direct compression (DC) method of producing tablets is taken into consideration, this is frequently quite true. DC is a cost-effective method of producing tablets that requires fewer unit operations for tableting, eliminating the need for labor-intensive process validation processes that are usually required for tableting using roller compaction or wet granulation (Schweikhart and Dembe, 2009). However, a large number of single-component excipients (SCEs) and active pharmaceutical ingredients have intrinsic rheological deficiencies, which limits the best use of direct compression for tableting because DC has strict requirements for materials with efficient physicomechanical functionality (Nenni et al., 2014). As a result, only a small portion of pharmaceutical excipients can be used in the direct compression process to produce

tablets with acceptable QTPPs (Armstrong, 2007). To address the shortcomings of current SCEs, new high functionality excipients would be required in order to fully realize the manufacturing potential of tableting by direct compression (Carlin, 2008). Novel excipients must undergo the same degree of scrutiny as novel medication molecules for human safety evaluation because they are regarded by regulatory authorities as new chemical entities (NCEs) and because there is no separate regulatory pathway for their development (Kozarewicz and Loftsson, 2018). Because the development of NCEs is surrounded by complicated scientific, economic, and regulatory difficulties (Bolhuis and Armstrong, 2006), this route is commercially non-rewarding for excipient development.

A more likely approach to creating novel tableting excipients is to functionally alter currently available SCEs that have regulatory safety profiles that have been established and are classified as Generally Recognized as Safe (GRAS)(Thoorens et al., 2014). Co-processed excipients, or excipient development consisting of a combination of two or more components combined in one frame through particle engineering, have become extremely popular in recent years. Particle engineering techniques, including co-processing, are investigated to produce unique co-processed excipients, which combine two or more GRAS listed excipients to produce new functionality for broader tablet manufacturing applications (Mirani et al., 2011; Carlin, 2008).

As a result, once created, co-processed excipients have regulatory influence over the synthesis of completely new chemical entities. According to reports, co-processed excipients outperform the corresponding SCEs in terms of critical tableting qualities (Rojas et al., 2012). Co-processed excipients are still scarce despite their availability, and their limited adaptability in direct compression stems from their set combination (Moondra et al.,2018).

To close this gap, it is necessary to create newer tableting materials. In order to meet the goals of the International Council for Harmonization of Technical Requirements for Registration of Medicines for Human Use (ICH), it is imperative that high-functioning, realistically priced, and novel co-processed excipients with demonstrated superiority over conventional excipients be developed. Process engineers and formulation scientists must use e-resources to speed up research and development and shorten time to market while simultaneously balancing quality and regulatory requirements. To overcome the known relatively poor compactibility of lactose, a co-processed excipient using a combination of lactose, mucin and corn starch BP was developed.

Diluents are frequently added to formulations in order to improve the active ingredient's bulk content and, consequently, the tablet's manageable size. The kind of plasticity and processing of the materials to be utilized will determine which diluent is best (Desai et al., 2012). Pharmaceutical tablets and capsules are frequently formulated with lactose as a filler or filler-binder. The general characteristics of lactose, such as its bland taste, affordability, low hygroscopicity, availability, compatibility with other excipients and active ingredients, excellent physical and chemical stability, and water solubility, all contribute to its appeal as an excipient (Emeje and Rodriguez, 2012).). Lactose was chosen as one of the ingredients of the tri-component excipient system. Another component of the system was corn starch BP, which is an established disintegrant that works by a combination of wicking and swelling as well as a bulking agent and a binder (Khainar et al., 2014). The third component, mucins, is essential to the defense mechanism of the gastrointestinal tract and to the dispersion of various mucins throughout the gastro-monogastric mammals. However, because to the high expense of discovering and developing new excipients, the distribution of mucin in polygastric animals is still mainly unknown. These are some of the issues that particle engineering must address (Mohammed et al., 2022; Momoh et al., 2012).

The active pharmaceutical ingredient (API) and excipients that can improve the functionality of the dosage form are frequently combined during the formulation of the pharmaceutical tablet. Ibuprofen, a chiral propionic acid derivative and member of the non-steroidal anti-inflammatory medicine (NSAID) class, is the recommended medication. Because of its analgesic, antipyretic, and anti-inflammatory properties, it is used to treat inflammatory disorders such rheumatoid arthritis, ankylosing spondylitis, mild osteoarthritis,

moderate pain, dysmenorrhea, vascular headaches, and fever. This work is targeted at formulating a tri-component co-processed excipient and evaluating its diluent performance in ibuprofen tablets obtained by direct compression and comparing with cellactose®, starlac® and anhydrous lactose as standard diluents.

Methods and Techniques

Materials

A predominantly plastic deforming excipient— Lactose anhydrous and a fairly elastic deforming excipient— corn starch BP powder (CDH Chemicals, India), were used as model primary excipients. Mucin was used as a binding agent during co-dispersion. Ibuprofen powder was obtained from Shasun Chemicals and Drugs Ltd. Magnesium stearate, crosspovidone, talc (Merck, Sigma-Aldrich) functioned as lubricating and flow enhancing agents. Two commercially available directly compressible co-processed excipients, Cellactose® (75% lactose monohydrate + 25% cellulose) and StarLac® (85% lactose monohydrate + 15% white native maize starch) graciously donated by Meggle Wasserburg GmbH & Co. KG, Germany, were used as reference standards for comparison.

Extraction of bovine mucin

With a few minor adjustments, the extraction of bovine mucin was done according to Mohammed et al.'s (2022) instructions. A recently slain cow's small intestines were split into short lengths, washed through with cold saline, and longitudinal sliced to reveal the mucosal surface. The mucus layer was carefully scraped off onto a microscope slide and placed into the cooled saline. Using cold acetone, the mucus was precipitated, and it was then air-dried. Using a milling machine, the resulting flakes were ground up and kept in an airtight container until needed.

Design of Experiments (DOE)

Determination of the precise amount of mucin and corn starch BP from 13 experimental runs of the excipients characterized using pharmacopoeial methods and standard procedures reported in the relevant literatures that would impart maximum hardness with minimum disintegration time was the key objective behind the implementation of DOE leading to the selection of the optimal ratio composition. Triplicate determinations were conducted, except otherwise specified.

Table 1: Experimental design for ratio optimization

Run order	Lactose (%)	Corn starch BP (%)	Mucin (%)	Disintegration time (min)	Hardness (KgF)
B1	90	1	9	17.49	12.0
B2	90	2	8	14.21	7.7
B3	90	3	7	6.23	4.0
B4	90	4	6	11.42	8.3
B5	90	5	5	7.09	10.3
B6	90	6	4	6.46	9.0
B7	90	7	3	5.23	5.7
B8	90	8	2	6.38	7.0
B9	90	9	1	3.3	8.0

Preparation of co-processed excipient composites

Using the co-dispersion method, the calculated amounts of the principal excipients (lactose, mucin, and corn starch BP) were triturated in distilled water to create composites in a ratio of 90:5:5. Over a digital water bath, controlled heating was maintained, with the system's interior temperature held at 40°C for 15 minutes. Two hours were spent convectively drying the co-dispersed slurry in a hot air oven chamber (Gallenkamp B.S 3, England). After being filtered through a 500-µm mesh screen, the moist mass was kept in a screw-capped bottle until needed again (Seville and Wu, 2016).

Tablet Preparation by direct compression technique

The formulation was prepared in four batches, as indicated in Table 2. With the exception of crosspovidone, talc, and magnesium stearate, the amount of each ingredient needed to make 200 tablets was determined and weighed out. It was then added using the doubling up technique, mixed until it was homogeneous, and tableted using a single station. The tablets were compressed to a target tablet weight of 500 mg using a Manesty tablet press, Model F-3 (Manesty, England), equipped with a set of flat faced punches (12.5 mm diameter) and dies at a compression pressure of 7 Metric tonnes.

Table 2: Formula for ibuprofen tablets

Ingredient	Batch 1	Batch 2	Batch 3	Batch 4
Ibuprofen (mg)	200	200	200	200
Co-processed excipient (mg)	270	-	-	-
Cellactose (mg)	-	-	270	-
Starlac (mg)	-	270	-	-
Lactose (mg)	-	-	-	270
Crosspovidone (mg)	21	21	21	21
Magnesium stearate (mg)	4.5	4.5	4.5	4.5
Talc (mg)	4.5	4.5	4.5	4.5
Total (mg)	**500**	**500**	**500**	**500**

KEY: Batch 1: CPE; Batch 2: Starlac; Batch 3: Cellactose; Batch 4: Lactose

Densities

Bulk (ρb) and tapped densities (ρt) were determined according to the procedure (measurement in a graduated cylinder) described in the United States Pharmacopoeia (2015) with modifications. The weight (w) of the sample material was divided by the loose volume (vb) it occupied in a 250 (±2) mL measuring cylinder to find (ρb). By tapping the cylinder 250–500 times on a hard, flat surface until a consistent volume (vt) was reached, the taped density (ρt) was found. The ratio of w to (vt) yielded the tapped density value.

$\rho b = \frac{w}{vb}$ …… (1)

$\rho t = {}^{w}/_{vt}$ …….. (2)

True density

The True density of each of the respective powder batches was determined by the solvent displacement method using xylene (Staniforth, 1988). Xylene was added to a 50 ml tarred pycnometer (W), and the weight was recorded as (W1). The xylene's weight was calculated by deducting W from W1. One gram of powder (W3) was added to the pycnometer bottle, the excess xylene that had been removed from the device was cleaned off, and the pycnometer's body was weighed once again (W4). Analogous calculations were conducted for every batch of ibuprofen powder. Equation (6) was used to calculate the True density, Pt. where V is the pycnometer's volume.

$Pt = [\frac{w3}{w1+w3} - w4]$ X S.G…….(3)

Hausner's ratio, Carr's index, and interparticle porosity

The Hausner's ratio (HR) and Carr's index (CI) were calculated from the bulk and tapped densities using Eqs. 1 and 2, respectively (USP, 2015).

$HR = \frac{\rho t}{\rho b}$ …… (4)

$CI = 100 - \frac{\rho t - \rho b}{\rho t}$ ……(5)

$$Ie = \left(\frac{\rho t - \rho b}{\rho t.\rho b}\right) \quad \ldots\ldots\ldots\ldots\ldots\ldots (6)$$

Angle of repose

A cotton-plugged glass funnel with 10 g of powder sample was held vertically on a retort stand, with its tip 7 cm from the base of an A4-sized plane sheet. This allowed for the measurement of the angle of repose, or σr. A powder pile with a height (h) and a diameter (d) developed on the sheet following the funnel's unblocking. ïr, which was obtained from Eq. 7, represents the angle formed by the inclined plane of the cone with respect to the base (Rojas et al., 2012).

$$Tan\,\Theta = \frac{h}{r} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots (7)$$

where h' and r' are respectively the means of triplicate measurements of the heights and radii of the cone measured along different axes.

Powder flow

Powder flow (t'') was measured using flowmeter (Erweka, Type GDT, Germany) as the rate at which sample weight (m) is discharged from the funnel compartment (Newmann et al., 2007).

$$Fr = \frac{weight\ of\ granules}{time} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots (8)$$

Particle size

Standard sieves were arranged one on top of the other in a stack so that sieves with bigger pores (fewer sieve numbers) are at the top and smaller pores (more sieve numbers) are at the bottom. The order of these sieves was ascending. A thirty-gram weight was added to the mesh. The sieve shaker has a 15-minute setting. In order to determine the amount retained in each mesh size and calculate the mean particle size, the sieves were taken out of the sieve shaker and weighed separately.

Fourier transform – infrared spectroscopy

With an IR spectrometer (Shimadzu FTIR 8400s, USA), the sample's Fourier Transform-infrared (FT-IR) spectra was recorded between 4000 and 650 cm-1. Potassium bromide (KBr) discs made from a sample mixture and dried KBr in a 1:200 ratio was used for this. The spectrum with the most distinct peaks was selected.

Quality Control of Tablets

Weight variation

Using an electronic balance, the weight of 20 randomly chosen pills was measured both collectively and individually. The weight of the tablets was then averaged. It was established how much each tablet's weight varied from the mean.

Friability test

A soft brush was used to remove any loose dust after ten pills were chosen at random and put on a sieve. The tablets that had been dedusted were weighed and then set on the friabilator's drum, which circulated for four minutes at a speed of 25 rpm. After dedusting, the tablets were weighed again. The following formula was used to calculate the % friability:

$$\%\ Friability = \frac{Initial\ weight - final\ weight}{Initial\ weight}\ X\ 100 \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (9)$$

Crushing strength test

Using the Monsanto hardness tester, the crushing strength of each of the ten tablets was ascertained for each batch, and the mean crushing strength was recorded.

Disintegration test
Six tablets, randomly chosen from each batch, had their individual disintegration rates measured using the basket method in an Erweka apparatus that was specified by B.P. (2012), using 0.1 N HCL in a medium at 37 ± 0.5°C. It was calculated what the mean disintegration time was.

Preparation of 0.2 N NAOH
Using a weighing balance, 2.0 grams of NaOH were weighed and then dissolved in 1000 milliliters of distilled water in a beaker. The solution was there once the 250 ml was prepared (Howard, 2007).

Preparation of 6.8 pH phosphate buffer
In a 1000 ml volumetric flask, a 6.8 g crystal of potassium dihydrogen phosphate was dissolved in 250 ml of distilled water and made up to volume. The pH was then adjusted to the necessary pH value of 6.8 using an electronic pH meter and the generated 0.2 N sodium hydroxide solution. The buffer was appropriately preserved for later usage after being meticulously packed with aluminum foil (Howard, 2007).

Preparation of standard calibration curve
200 milligrams of pure ibuprofen powder were added to a 100 milliliter volumetric flask, which was then filled with the same solvent and dissolved using a pH 6.8 potassium dihydrogen phosphate buffer. The solvent was diluted 1 in 10 ml, and the absorbance at 221 nm was measured using a UV spectrophotometer. Plotting an absorbance versus concentration (mg) standard calibration curve.

Dissolution
USP equipment 11 was used to measure the rates at which the active ingredient in the tablets dissolved (paddle). The dissolution jars were filled with a 900 ml volume of newly made dissolution medium (pH 6.8 phosphate buffer) and kept at 37 ± 0.5°C. The result was a 50 rpm rotation of the paddles. The tablet from each batch was then put in the basket, and at 10, 20, 30, 40, 50, and 60 minutes, a 10 ml sample was taken out and subjected to spectrophotometric analysis at a wavelength of 221 nm to determine the concentration of ibuprofen. Ten milliliters of new aliquots of the dilution medium were substituted for the samples removed for analysis, and the percentage of drug released was computed as follows:

Absorbance = Slope × concentration ± intercept …… (10)

$$Percentage\ drug\ release = \frac{Amount\ released\ at\ time\ (t)}{Dose\ (mg)}\ X\ 100 \quad \ldots\ldots\ldots\ldots\ldots\ldots (11)$$

Statistical analysis
One-way analysis of variance (ANOVA) was used in the statistical analysis, which was performed using IBM SPSS version 21 (SPSS Inc., Chicago, Illinois, SA) software. At $p < 0.05$, the results were deemed significant.

Results
Table 3: Powder Analysis of Single Components

Parameter	Lac	Ms	Muc
Angle of repose (o)	45.13(1.53)	38.55(1.00)	13.68 (0.03)
Bulk density (g/ml)	0.28(0.02)	0.26(0.03)	0.35(1.1)
Tapped density (g/ml)	0.33 (1.2)	0.33(0.31)	0.38(0.9)
Carr's index (%)	16.71(0.52)	21.02(1.5)	7.18(6.3)
Hausner's ratio	1.20(8.5)	1.27(4.2)	1.08(3.7)
Flow rate (g/sec)	0.55(0.3)	1.04(1.1)	3.47(1.2)

KEY: **Lac**: Lactose; **Ms**: Maize Starch; **Muc**: Mucin

Table 4: Powder analysis of co-processed excipient

Analysis	CPE
Angle of repose (o)	18.43
Bulk density (g/ml)	0.40
Tapped density (g/ml)	0.42
Carr's index (%)	3.98
Hausner's ratio	1.04
Flow rate (g/sec)	2.02
True density	1.50
pH	6.5

Table 5: Micromeritic properties

Parameter	Batch 1	Batch 2	Batch 3	Batch 4
Angle of repose (O)	29.76 ± 0.53	29.00 ± 1.00	34.10 ± 0.10	31.33 ± 1.16
Bulk density (g/ml)	0.38 ± 1.01	0.39 ± 0.01	0.39 ± 1.11	0.39 ± 0.01
Tapped density (g/ml)	0.48 ± 0.01	0.49 ± 0.01	0.48 ± 1.21	0.48 ± 0.01
Carr's index (%)	20.80 ± 0.01	20.40 ± 0.01	20.40 ± 0.01	20.40 ± 0.10
Hausner's ratio	1.26 ± 0.60	1.26 ± 0.40	1.23 ± 0.10	1.23 ± 0.30
Porosity (%)	74.10 ± 0.60	74.00 ± 0.56	74.00 ± 0.54	74.02 ± 0.40
Flow rate (g/sec)	4.67 ± 0.21	3.83 ± 0.06	3.50 ± 0.06	3.63 ± 0.06
Particle size (µm)	279	220	173	269
True density (g/ml)	1.48 ± 0.20	1.50 ± 0.01	1.49 ± 0.10	1.51 ± 0.02

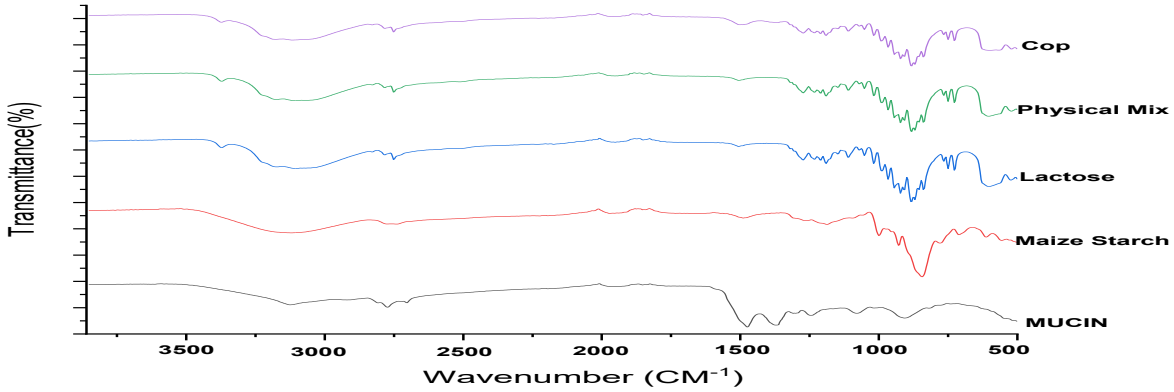

Figure 1: FTIR overlay spectra

Table 6: Tablet properties evaluated

Parameters	Batch 1	Batch 2	Batch 3	Batch 4
Mean tablet weight (g)	0.51(8.79)	0.51(8.64)	0.51(13.51)	0.51(7.57)
Thickness (mm)	3.95(2.3)	3.83(2.1)	3.89(1.22)	3.81(1.10)
Diameter (mm)	12.12(1.34)	12.04(0.31)	12.10(2.11)	12.09(1.31)
Crushing strength (KgF)	6.67(0.72)	8.00(0.54)	8.00(0.56)	7.00(1.03)
Tensile strength (Nm^{-2})	0.89	1.10	1.08	0.97
Friability (%)	0.80(0.00)	0.97(0.07)	0.94(0.00)	0.54(0.04)
Disintegration time (sec)	24.67(0.35)	31.33(2.11)	17.67(1.26)	17.33(1.6)
HFR	8.34	8.24	8.51	12.96

KEY**: Batch 1**: CPE; **Batch 2**: Starlac; **Batch 3**: Cellactose; **Batch 4**: Lactose ; **HFR**: Hardness friability ratio

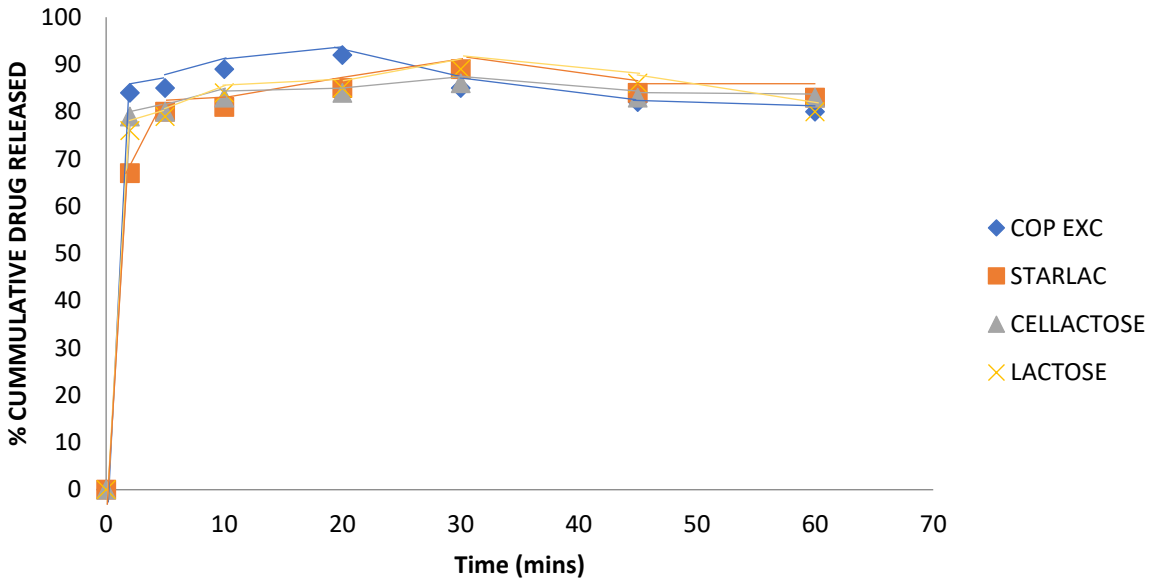

Figure 2: Plot of percentage drug released against time

Discussion

Design of experiments

It is challenging to enhance a single excipient's particular qualities without sacrificing its other functions since they may be incompatible. For example, improving compactibility may have an impact on the system's capacity to disintegrate. Coprocessed excipients help to overcome these challenges and provide better multifunctional qualities than single ones (Rojas *et al.,* 2012).

To counteract lactose's generally poor compactibility, a coprocessed excipient was created, consisting of a mixture of lactose, mucin, and maize starch BP. The main goal of implementing DOE was to precisely determine how much mucin and corn starch would give greatest hardness with minimum disintegration time. Based on a quadratic model that included both linear and interaction terms of independent variables to explain the experimental data, B5, with a crushing strength of 7.09 KgF and a disintegration time of 10.3 sec, produced the best result (optimum ratio) for both hardness and disintegration time. These experimental results are displayed in Table 1 (Latchubugata et al., 2018). Table 4 demonstrated better and enhanced flow properties from Tables 3 and 4, which represent the solo components and the coprocessed excipients, respectively. This indicates that coprocessing two or more excipients improves flow and compressibility (Mohammed *et al*., 2005).

Densities

Table 5 displays the findings of the assessments of the ibuprofen formulations' bulk and tapped densities. For all of the ibuprofen batches containing co-processed excipient, starlac, cellactose, and lactose, the bulk densities were consistently lower than the tapped densities (Daraghmeh et al., 2010). This suggests that the powder bed's volume decreased upon agitation. They fall within the category of compressible granules as a result. The bulk densities did not differ significantly ($p > 0.05$). The tapped densities showed an identical pattern.

True density

True density is a fundamental material feature that is crucial for comprehending the mechanical characteristics and compaction behaviors of pharmaceutical powders. According to Goh et al. (2018), true and envelop densities are required to compute the porosity of a solid specimen. For instance, because it is

not affected by changes in tableting speed, the link between tablet porosity and tensile strength can be helpful in directing scale up (Daraghmeh et al., 2010). The real density data from Table 5 showed that there was no discernible change, ranging from 1.48 ± 0.20 to 1.51 ± 0.02.

Flow rate

Table 5 displays the outcomes of the different batches' flow rates. In comparison to the other batches, batch 1 (co-processed excipient) had the highest flow. According to Katdase and Chaubal (2006), the granules exhibited favorable flow characteristics and may be utilized to produce ibuprofen tablets with consistent weight, hardness, and content.

Angle of repose

Solid flow qualities have been described using the angle of repose. The barrier to particle movement or interparticulate friction is typically associated with angle of repose. Table 5 displays the batches' angle of repose, which varied between 29.00 ± 1.00 and 34.10 ± 0.10. The angle of repose of batches containing cellactose and lactose differed significantly ($p < 0.05$). Nonetheless, no statistically significant distinction ($p > 0.05$) was seen between the batches that contained starlac and co-processed excipient. In general, the powders can be categorized as having an outstanding flow (Gohel et al., 2007; Kumar and Koh, 2012). They would fill the dies correctly during tableting because of their flowability, producing tablets with little weight fluctuation.

Hausner's quotient and Carr's compressibility Index

The ranges for the various batches' Hausner's quotient and Carr's compressibility index were 1.23 ± 0.10 - 1.26 ± 0.40 and 20.40 ± 0.01 - 20.80 ± 0.01 %, respectively (Table 5). Good flow qualities can be applied to the powders in general (Ansel et al., 2011; Kunle, 2019). These flow indices imply that, in order to facilitate the manufacture of well-filled and compressed tablets, the powder mix would be logically discharged from the hopper to the die.

Porosity

The findings of the ibuprofen tablets' porosity evaluation is found on Table 5. The porosity values validate non-cohesiveness, hence supporting the good flow that was noted. For optimal die filling and the creation of tablets with little weight variation, powders should have adequate flowability. Their porosities did not exhibit any discernible changes. This aligns with the findings of Ilic et al. (2009).

FTIR

The FTIR overlay spectra are displayed in Figure 1. Lactose was the predominant excipient, as indicated by the majority of peaks in the final spectra (Co-processed excipient). The physical mix and the co-processed excipient all reflected the aliphatic C-H stretch, OH stretch bond, and C-O stretch at the same wavenumber, suggesting that a small amount of heating of the co-processed excipients was insufficient to produce a noticeable chemical interaction or chemical change (Daraghmeh et al., 2010).

Particle size

The impact on densities and flow characteristics can be further explained by the fact that the particle size range is between 173 and 279 μm (Mirani et al, 2011).

Crushing strength

An essential in-process test called crushing strength measures the power needed to break or crush a tablet and determines if the tablets are made with enough firmness to resist breaking, chipping, or crumbling, but not too much so as to cause disintegration to occur more slowly. The main function of binders is to provide solid particles the cohesion they need to link together during compaction to form tablets. By increasing intra- and intergranular forces, binders have the potential to increase the hardness of tablets. The range of values that can be achieved for tablet crushing strength is 4-8 kgF. This is because too much binders and compression pressure can cause the compressed tablets to become excessively hard, which can prevent them from disintegrating in the intended amount of time. Therefore, it is necessary to regulate binder concentration to avoid producing both soft tablets that cannot tolerate handling stress and too hard tablets

that would hinder absorption or cause tablets to be excreted unchanged. According to Table 6's results, Batches I through IV passed the hardness test because their results were within the acceptable range.

Friability

Another mechanical characteristic of tablets that is stated in the official compendia is friability, which should not be greater than 1.0%. It is a surface deformation of tablets caused by the tablet's morphology; the more abrasive the tablet's surface, the more friable it would be. It is noteworthy, nonetheless, that the tablet batches that were below the 1% restriction in Table 6 passed the friability test. This is consistent with the crushing strength and could also be attributable to the compression pressure. Since none of the tablets exceeded the pharmacopoeia criteria of 5%, they all passed the uniformity of weight test (BP, 2012).

Disintegration test

The disintegration test counts the number of milliseconds it takes for a tablet to fragment into smaller particles, or granules, in this instance in physiological media. It is a crucial phase in the medication release process from prescription dose forms. The British Pharmacopoeia stipulates that uncoated tablet breakdown takes fifteen minutes. The tablets' disintegration resulted in a short mean disintegration time of less than 5 minutes when compared to directly compressed tablets; in fact, it happened in seconds (17.33 sec to 31. 33 sec). This complements the results of the crushing strength and friability.

Thickness and diameter

Table 6 displays the ibuprofen pills' thickness and diameter. The diameter and thickness of the various tablets do not significantly differ from one another ($p > 0.05$). This implies that the granules were fairly uniformly filled into the dies and that the compression pressure applied to the granules during tableting was uniform.

Hardness friability ratio

One metric used to evaluate the mechanical strength of the tablets in relation to the potential effects of abrasive activities on the tablet is the hardness friability ratio. According to Table 6, the ibuprofen tablets were ranked in the following order of strength: Batch IV > Batch III > Batch I > Batch II (lactose > cellactose > coprocessed excipient > starlac, respectively). This supports the idea that a tablet's strength increases with its HFR score.

Dissolution study

A dissolution research can provide some information into how a medicine releases from a dosage form. It is employed as a less direct way to gauge medication availability, particularly when evaluating manufacturing processes and formulation elements that could have an impact on bioavailability. Every batch had a satisfactory tablet release and dissolution profile, according to the tablet release profile result (Fig. 2). This was the case for all batches, as in just two minutes, more than 60% of the medication was released. Additionally, the largest release of CPE was observed at 20 minutes, followed by lactose and starlac at 30 minutes, and cellactose at 30 minutes. For every batch, there was a rapid release of ibuprofen (T50%) from the tablets within two minutes. Subsequently, the release rose progressively until thirty minutes, at which point it started to decrease. Every batch complied with the BP guidelines, which state that the pills must release up to 50% of the ibuprofen within 30 minutes (BP, 2012).

Conclusion

A novel coprocessed excipient (CPE), which is a combination of lactose, mucin, and corn starch, was created as a diluent to be used in direct compression for tableting purposes. Using DOE, the best possible combination of CPE—90% lactose, 5% mucin, and 5% corn starch BP—was determined. When compared to the component parts, the developed CPE had better density and flow characteristics. Lactose is an excellent option for direct compression because of its homogenous range of particle sizes, reduced moisture content, and increased cohesivity.

It was determined that the developed tri-component coprocessed excipient was desirable for further use in pharmaceutical formulations based on comparative in-vitro drug release data with formulations of existing

coprocessed diluents. As a result, a combination of these excipients may have considerable potential and financial advantages, making it a trustworthy alternative to common diluents, particularly when making traditional tablets.

Acknowledgement
This work was funded under the Institution Based Research, TETFUND Research Grant of Kaduna State University, KASU.

Conflict of interest
The authors declare that there is no conflict of interest.

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