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Evaluation of the sustained release properties of hydroxypropylated cassava and potato starches in diclofenac tablet formulations

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Abstract

Hydroxypropylation of starch enhances its potential applications, especially its use in specialized drug delivery systems. The study aimed at exploring the sustained release property of hydroxypropylated (HP) cassava and potato starches in diclofenac sodium tablet formulations. Native cassava and potato starches were hydroxypropylated and used in the preparation of batches of diclofenac powder blends and granules either as powders (filler) or mucilage (binder). Powder blends/granules flow properties were investigated as well as drug-excipient interaction using Fourier transform infra-red spectroscopy prior to tablet compression. Compressed tablets were evaluated for tablet properties and *in vitro* drug release was compared with a commercial brand. Drug release kinetics and mechanisms of the tablets were determined from the dissolution profiles. Powder blends and granules containing HP starches exhibited excellent flow properties. Drug-excipient studies showed the absence of any interaction. Formulated tablets had uniform weights with concentration-dependent hardness for those prepared with HP starch mucilage and were stronger than those prepared with HP starch powder via direct compression. Tablets incorporated with HP starch mucilage produced non-friable tablets (≤ 1%) while those prepared with powder blends were highly friable (10.00 and 11.39 %). Drug release from the tablets was sustained ranging from 43.60 - 81.67% within 8 h and comparable with that of the commercial brand (44.38%). Kinetics of drug release followed first-order with Hixson-Crowell mechanism of release while the commercial brand favoured zero-order kinetics. The study showed that hydroxypropylated cassava and potato starches have potential to retard the rate of drug release in tablet formulations.

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INTRODUCTION

Chemical modification of starch involves the introduction of functional groups to its molecule, thereby creating varied physico-chemical characteristics, controlled by the reactivity of the glucose residue (Cornejo-Ramírez *et al.*, 2018). The derivations are generally achieved through esterification, etherification, crosslinking, cationization, oxidation, and grafting (Gałkowska *et al.*, 2018; He *et al.*, 2023). The achievable functional characteristics depend largely on the biological source of the starch, which in turn determines the granular size and structure, as well as internal pores and cavities (Zhu *et al.*, 2024).

Studies have shown the various potential effects of chemical modifications on starches. These include the influence on rheological and pasting properties as well as the morphological and thermal characteristics (Olayinka *et al.*, 2015; Guleria and Yadav, 2022; Paramasivam *et al.*, 2023). In addition, the chemical treatment of native granular starches has been reported to alter the intrinsic behavior of the starches, in terms of gelatinization, retrogradation and pasting (Karim *et al.*, 2008; Mohamed, 2021). Chemically modified starches have demonstrated significantly better level of smoothness, paste consistency, freeze-thaw and cold storage stability over their native, unmodified counterparts (Singh *et al.*, 2007; Korma *et al.*, 2016; Rashwan *et al.*, 2024). Some of the factors that influence starch modification rate and efficiency include granule morphology, ratio of amylopectin to amylose, type as well as concentration of the modifying reagent used (Guleria and Yadav, 2022; Compart *et al.*, 2023; El-Farkhani *et al.*, 2024).

Hydroxypropylation is a frequently adopted chemical modification method, because of the enhanced thermal characteristics upon gelatinization. These products are created via a substitution reaction, where the hydroxypropyl functional groups displace atoms on the native starch molecule in the presence of alkali catalysts (Senanayake *et al.*, 2014). The resulting derivatized granular structure has improved functionalities, including enhanced freeze-thaw stability and paste clarity, reduced temperature of gelatinization and elevated values for peak viscosity (Shen *et al.*, 2021; Choi and Kim, 2022). The aim of this study was to evaluate the release retardant potential of hydroxypropylated cassava and potato starches in diclofenac sodium tablet formulations.

MATERIALS AND METHODS

Diclofenac sodium (Surechem Products Ltd, Suffolk England), concentrated hydrochloric acid (BDH Chemicals Ltd, Poole, England), potassium hydrogen phosphate and sodium hydroxide (Merck, Germany) were used as procured from local suppliers. Diclofenac sodium 100 mg tablets (Clofenac SR®, Hovid Bhd., Malaysia) were purchased from a registered pharmacy outlet in Benin City, Nigeria.

Starch extraction, hydroxypropylation and characterization

Extraction of cassava and potato starches, hydroxypropylation of the starches as well as the characterization of the hydroxypropylated (HP) products have been previously reported (Mudiaga-Ojemu *et al.*, 2023).

Preparation of powder blends/granules

The formula used in the preparation of twelve (12) batches of diclofenac sodium powder blends/granules is shown in Table 1. Two (2) powder blends batches (C1 and P1) were prepared using hydroxypropylated (HP) cassava and potato starch powders only while granules of the other batches were prepared with a combination of native and HP starches, either in powder form or mucilage, using the wet granulation method. Granules were prepared by wet massing the diclofenac sodium powder and diluent (native or HP starch powders) in a mortar with sufficient quantities of the native or HP starch mucilage (%w/v).

The wet mass produced was screened through a sieve (2-mm mesh size) then dried in a hot air oven (Gallenkamp, UK) at 60 °C for 30 min. The granules were further screened through a sieve of 710 µm mesh size and dried again at 60 °C for 60 min. The dried granules were packaged in an airtight container and stored in a desiccator until use.

Table 1. Composition of diclofenac sodium powder blends/granules

Batches		Ingredients (mg)				
		Diclofenac sodium	HP starch powder	HP starch mucilage	Native starch powder	Native starch mucilage
Cassava starch	C1	100	200	-	-	-
	C2	100	150	50	-	-
	C3	100	100	100	-	-
	C4	100	50	150	-	-
	C5	100	-	200	-	-
	C6	100	-	-	100	100
Potato starch	P1	100	200	-	-	-
	P2	100	150	50	-	-
	P3	100	100	100	-	-
	P4	100	50	150	-	-
	P5	100	-	200	-	-
	P6	100	-	-	100	100

Powder blends/Granule analysis

Bulk and tapped densities

The volume occupied by 50 g of powder blends or granules in a 100 mL measuring cylinder was noted bulk volume while the volume occupied by the powder blends or granules in the same measuring cylinder after tapping 50 times on a flat surface was noted as the tapped volume. Bulk and tapped densities were calculated by dividing the weight of powder blends or granules with their respective volumes.

Carr's compressibility index and Hausner's ratio

These parameters were calculated as the difference between tapped and bulk densities, divided by the tapped density and expressed as a percentage was recorded as the Carr's index while the ratio of the tapped to bulk density was calculated as the Hausner's ratio.

Flow rate

The time taken for the powder blends or granules (50 g) to flow through a funnel was noted and the flow rate was calculated as the ratio of the granule weight to the time taken (g/sec).

Angle of repose

The powder blends or granules (50 g) were poured into a funnel whose orifice had been plugged, the height and diameter of the heap formed after opening the orifice of the funnel were measured and used in calculating the angle of repose (θ) using the equation below;

$$\text{Angle of repose } (\theta) = \tan^{-1}(h/r) \quad (1)$$

Where h is the height of the heap of powder blends or granules and r is the radius of the circular base

Drug-excipient interaction studies

Drug excipient compatibility study was carried out with a pure sample of diclofenac sodium powder and formulated batches of the powder blends/granules. The FTIR spectra of the formulated powder blends/granules was compared with that of the pure sample of diclofenac sodium powder.

Compression of powder blends/granules

The prepared powder blends and granules were compressed into tablets using a rotatory punch tableting press (F3-Manesty, Manesty Machine Ltd, England) at a compression pressure of 25 arbitrary unit load of pressure. All the tablets were kept for 24 h before evaluation to allow for elastic recovery.

Evaluation of tablets

The diclofenac sodium tablets formulated were evaluated of the following physicochemical parameters; weight and dimension uniformity, hardness, friability as well as dissolution time.

Uniformity of weight and dimension

Twenty (20) tablets from each batch were randomly selected and weighed with an electronic balance (Scout-Pro, China). Subsequently, the respective mean and standard deviations values were calculated. A micrometer screw gauge (Sterling Manufacturing

Company, England) was then used to determine the tablet thickness and diameter, then the mean as well as standard deviation values were processed (British Pharmacopoeia, 2003).

Tablet hardness

The tablet hardness was determined using a motorized digital hardness tester (Campbell Electronic Hardness Tester, Model HT 3050, India). This assessment was performed by determining the load required to cause diametric fracture of 10 tablets randomly selected from the individual batches, and the mean values computed.

Tablet friability

The friability test was performed by weighing ten (10) randomly selected tablets from each batch. The tablets were dedusted and placed in the drum of an Erweka Friabilator (Erweka, Germany) and treated to free fall and cascading stress for 4 min, at the rate of 25 rpm. Subsequently, the tablets were removed, dusted again and weighed to ascertain the percentage weight loss (British Pharmacopoeia, 2003).

Dissolution studies

Dissolution was performed *in vitro* using US Pharmacopoeia Dissolution Type II apparatus containing 900 mL dissolution medium which was maintained at 37 ± 0.5°C and set to run at 50 rpm. Two (2) tablets randomly selected from the formulated batches of tablets was used for the test. The first stage of the test was run in 0.1 M HCl for 2 h, aliquots of 5 mL were withdrawn at intervals of 10, 25, 40 min and then at 1.0 and 2 h. Fresh medium was used to replaced withdrawn aliquots to maintain sink conditions. Afterwards, the dissolution medium was replaced with 0.1 M phosphate buffer (pH 8.0) and run for 6 h. Aliquots were also withdrawn at pre-determined times of 3, 4, 6 and 8 h and equal volumes of fresh medium were also used to replaced withdrawn aliquots. Absorbances of the withdrawn samples were obtained from the UV visible spectrophotometer at 316 nm (T70, PG Instruments Ltd, UK).

The amount of drug released per time was computed from the standard calibration curve developed from the pure diclofenac sodium. The test was repeated for a commercial diclofenac sodium sustained release tablet (Brand Z).

Release kinetics

Drug release data obtained from the dissolution tests were fitted into various kinetic equations to determine the model and mechanism of diclofenac sodium release from the tablets. The models employed were zero order, first order, Higuchi, Hixson-Crowell and Korsmeyer Peppas according to the following equations.

$$Q = kt \text{ (zero-order equation)} \quad (2)$$

$$\ln (1-Q) = -kt \text{ (first-order equation)} \quad (3)$$

$$Q = kt^{1/2} \text{ (Higuchi equation)} \quad (4)$$

$$Q^{1/3} - Qt^{1/3} = kt \text{ (Hixon Crowell equation)} \quad (5)$$

$$\log Q = \log k + n \log t \text{ (Korsemeyer-Peppas equation)} \quad (6)$$

Where, Q is the fraction of drug released at time t, k is the release rate constant and n is the diffusional exponent. The correlation coefficient (r^2) from plot of each equation was calculated. Drug release profile was considered to follow a particular rate order or mechanism if the r^2 value was ≥ 0.9.

Statistical analysis

Descriptive statistics were performed for all data using GraphPad Instat (v. 3.06). Therefore, the mean and standard deviations of all replicate determinations were computed and reported, and the differences between means were determined using one One-way analysis of variance (ANOVA), where $p < 0.05$ were considered significant.

RESULTS AND DISCUSSION

Flow and bulk properties of powder blends/granules

The flow properties of the prepared granules and powdered mixtures are presented in Table 2. Granules prepared with highest concentration of starch in mucilage (Batches C5 and P5) had the highest flow rate (5.24 and 5.52 g/sec) compared to

other granules prepared with less amount of starch in mucilage. Batches C6 and P6 prepared with the native cassava and potato starches respectively were found to have the least flow rate (2.15 and 2.05 secs respectively).

Meanwhile, Batches C1 and P1 containing powder mixtures of diclofenac sodium and hydroxypropylated cassava and potato starches had high flow rate (5.16 and 5.57 g/sec) indicating faster flow time. Hydroxypropylation of the starches is observed to enhance dry powder flow similarly, incorporation of high concentration of HP starches also improved flow of diclofenac sodium granules over those granules prepared with the respective native starches.

The angle of repose is an indirect measurement of the flow of materials, values < 30° indicate excellent flow, values from 31° to 35° indicate good flow, values from 36° to 40° and those > 40° signify material with fair and poor flow respectively (Chavez-Salazar *et al.*, 2017). Table 2 shows that angle of repose of cassava starch formulations were between 16.58 and 30.34° while those of potato starch formulations were between 18.36 and 44.38°. The powder mix of HP starches were observed to have better flow than the granules prepared with HP starches.

Table 2. Micromeritics properties of diclofenac powder blends/granules

Batches	Bulk density (g/ml)	Tapped density (g/ml)	Carr's index (%)	Hausner's ratio	Angle of repose (°)	Flow rate (g/s)
C1	0.69 ± 0.03	0.80 ± 0.05	13.81 ± 0.67	1.16 ± 0.00	19.93 ± 1.64	5.16 ± 0.19
C2	0.55 ± 0.00	0.66 ± 0.01	16.64 ± 3.22	1.20 ± 0.05	22.11 ± 2.01	4.83 ± 0.33
C3	0.56 ± 0.00	0.66 ± 0.01	15.28 ± 1.96	1.18 ± 0.03	21.61 ± 0.21	4.34 ± 0.10
C4	0.56 ± 0.00	0.64 ± 0.01	12.50 ± 1.96	1.14 ± 0.03	24.27 ± 0.25	3.60 ± 0.05
C5	0.61 ± 0.03	0.68 ± 0.02	10.48 ± 5.98	1.12 ± 0.07	16.58 ± 1.42	5.24 ± 0.16
C6	0.66 ± 0.00	0.71 ± 0.00	7.59 ± 0.43	1.08 ± 0.01	30.34 ± 0.61	2.15 ± 0.01
P1	0.74 ± 0.04	0.82 ± 0.02	9.56 ± 2.64	1.10 ± 0.03	18.36 ± 0.92	5.57 ± 0.4
P2	0.60 ± 0.01	0.66 ± 0.02	8.96 ± 0.19	1.10 ± 0.00	20.07 ± 1.14	5.10 ± 0.16
P3	0.61 ± 0.03	0.65 ± 0.06	6.16 ± 4.55	1.07 ± 0.05	20.00 ± 2.17	4.28 ± 0.12
P4	0.59 ± 0.02	0.63 ± 0.03	5.89 ± 0.24	1.06 ± 0.00	20.69 ± 1.99	4.26 ± 0.09
P5	0.56 ± 0.01	0.66 ± 0.06	14.98 ± 5.48	1.18 ± 0.08	29.81 ± 0.30	5.52 ± 0.09
P6	0.62 ± 0.00	0.69 ± 0.00	9.97 ± 0.83	1.11 ± 0.01	44.38 ± 1.32	2.05 ± 0.00

However, all formulations containing the modified starches (whether dry powder or granules) had excellent flow; they were free flowing compared to granule formulations prepared with native cassava starch which demonstrated free flow properties (30.34°) and native potato starch which had fair to passable flow (44.38°). It is necessary for materials to be compressed into tablets to be free flowing because materials with poor flow would not flow properly from the hopper into the die cavity resulting to inconsistent tablet weights and inconsistencies in bioavailability.

Hausner's ratio (HR) and Carr's index (CI) show the cohesive nature of materials and their propensity to decrease upon application of pressure as seen in the tableting process. Materials with HR ≤ 1.11 are termed cohesive while those with values between 1.12 and 1.20 are less cohesive (Lawal *et al.*, 2016). Batches prepared with HP cassava starch were less cohesive than those prepared with HP potato starch. Dry powder formulations of C1 and P1 had similar HR (1.16 and 1.11 respectively) which were also less cohesive than those prepared with the native starches; C6 and P6 with HR values of 1.08 and 1.11 respectively. Formulations prepared with HP potato starch showed better propensity to be easily deformed under pressure (CI values between 5.89 and 14.98 %) than those prepared with HP cassava starch (10.48 and 16.68%). Hydroxypropylation is observed to reduce the cohesive nature of the formulations indicating lower degree of densification and improved flow (Odeku and Picker-Freyer, 2009).

Drug-excipient interaction studies

FTIR spectrum of pure diclofenac sodium showed an absorption peak at 3244.00 cm^{-1} corresponding to

stretching of carboxylic group and the peak at 1562.81 cm^{-1} linked to C=O stretching of the carboxyl ion was also observed. The absorption peak at 1458.05 cm^{-1} corresponding to C = C ring stretching and another at 758.11 cm^{-1} were also observed. These characteristic absorption peaks and bands are characteristic of diclofenac sodium (Shivakumar *et al.*, 2008; Edavalath *et al.*, 2011) showing that the diclofenac sodium powder used was of pure quality.

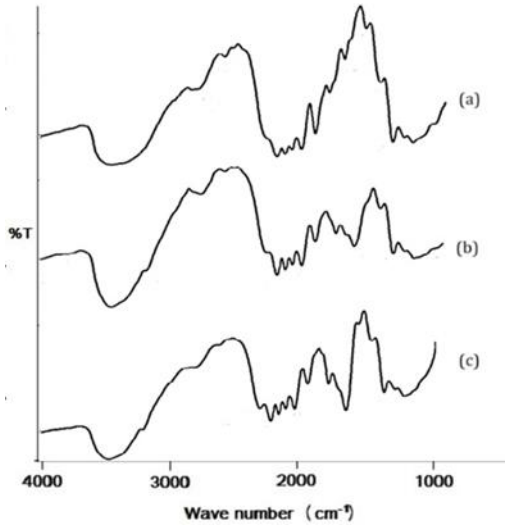

Fig. 1. FTIR spectra of diclofenac sodium powder (a) and tablet formulation of HP cassava starch (b) and HP potato starch (c)

The peak corresponding to stretching of O-H stretching at 3424.00 cm^{-1}observed in Fig. 1a is seen to be slightly increased and sharper at 3432.00 cm^{-1} and 3430.00 cm^{-1} in Figs 1b and 1c respectively as a result of hydroxypropylation. Absorption peak corresponding to C-H stretch at 2957.00 cm^{-1} and 2946.00 cm^{-1} is observed to be prominent and sharp in Figs 1b and 1c respectively. Band broadening and sharp peaks observed in the spectrum of the modified starches indicate stronger hydrogen bonding due to incorporation of etherification groups as a result of hydroxypropylation (Iftikhar *et al.*, 2022; Mudiaga-Ojemu *et al.*, 2023).

In addition to the inclusion of specific groups associated with hydroxypropylation, no other new peaks were observed nor was there disappearance of any characteristic peaks due to the drug. This indicates the absence of any interactions between drug and excipient and also confirms the compatibility of diclofenac sodium with the modified excipients present in formulation.

Physicochemical properties of diclofenac tablets

Table 3 shows the physicochemical properties of diclofenac tablets formulated using the hydroxypropylated starch at different binder concentrations and also those tablets made using the native starch. Uniformity of weight is an important parameter that establishes even distribution of ingredients within a tablet dosage form. Tablets with uniform weights indicate that there are no inconsistencies in tablet doses and minimal/no problems in bioavailability of the active ingredient. There was no significant difference between tablet weights of all the batches ($p < 0.0001$) which was congruent with the official specifications (British Pharmacopeia, 2003) for tablets with average weight of 300 mg. The result shows that both the native and hydroxypropylated starches are capable of being compressed under pressure without variation in tablet weights.

Hardness test assesses the structural integrity and robustness of tablets with respect to processes during manufacturing, transportation, storage and patient use. Hardness values between 4 and 8 kgF are stipulated as optimum for uncoated tablets for immediate release (Odeku and Itiola, 2003). Batches C1 and P1 prepared by direct compression and containing no mucilage had lower hardness (3.60 and 3.33 kpa respectively) and can be ascribed to the fact that there was weak bonding between the particles leading to weak tablet structure.

Batches prepared with the native starches (batches C6 and P6) had hardness exceeding values measurable by the hardness tester, probably due to high amount of the native starch mucilage. For batches C2 - C5 and P2 - P5, as the concentration of HP cassava and potato starch mucilage increased, tablet hardness was observed to increase due to increased particle-particle

contact as a result in presence of more binder mucilage concentration leading to creation of stronger particle bonds in the tablets (Koster and Kleinebudde, 2024). Table 3 shows that tablets prepared with HP cassava starch were stronger than those prepared with HP potato starch.

Friability assesses tablet weakness and gives an insight into the ability of the tablet to withstand abrasion, friction or mechanical shock. Friability positively correlates with tablet hardness in that, tablets with low hardness results in tablets with potentially high friability.

Table 3. Some physicochemical properties of formulated diclofenac tablets

Batches	Weight uniformity (g)	Hardness (kpa)	Friability (%)
C1	298.60 ± 1.76	3.60 ± 0.46	10.00 ± 0.20
C2	298.60 ± 1.84	8.63 ± 0.55	0.30 ± 0.05
C3	297.13 ± 2.33	10.73 ± 1.10	0.50 ± 0.05
C4	301.27 ± 2.89	10.63 ± 0.38	0.00 ± 0.00
C5	298.73 ± 1.49	9.93 ± 0.38	0.30 ± 0.05
C6	299.73 ± 3.33	> 15.00	0.33 ± 0.09
P1	301.33 ± 4.42	3.33 ± 0.58	11.39 ± 0.18
P2	300.20 ± 2.21	6.57 ± 0.60	0.79 ± 0.00
P3	299.27 ± 2.40	8.27 ± 1.02	0.40 ± 0.00
P4	300.47 ± 1.92	8.67 ± 0.29	0.40 ± 0.00
P5	299.47 ± 3.00	7.17 ± 0.29	0.50 ± 0.05
P6	299.60 ± 2.53	> 15.00	0.27 ± 0.09

Batches C1 and P1 with low hardness values were observed to have correspondingly high friability. This shows that formulation of tablets with HP cassava and potato starches by direct compression method yields soft and friable tablets. Conversely, incorporation of HP starch mucilage produced non-friable tablets with values between 0.00 and 0.79 across the different HP starches and different concentrations used which is within the acceptable limit of ≤ 1% (British Pharmacopeia, 2003). This shows that incorporation of HP starch mucilage resulted in strong particle-particle binding of the drug and starch which led to mechanically strong tablets. Results from this study is in contrast to that reported by Okunlola *et al.* (2017) where they reported that HP white yam starch produced highly friable tablets. It can therefore be deduced that hydroxypropylation of cassava and potato starches is capable of producing strong and robust tablets.

In vitro dissolution

Figs 2a and 2b show the release profile of the formulated diclofenac sodium tablets and the commercial brand of tablets (Z). All the tablets showed low release (< 20%) in 0.1 N HCl however in phosphate buffer medium, the tablets showed faster release but to varying degrees. Tablets prepared with native cassava and potato starches (Batches C6 and P6) gave the fastest release (about 70%) in phosphate buffer medium, showing that these natives starches do not have the capacity to prolong drug release. Tablets containing HP cassava starch prepared by direct compression (Batch C1) exhibited the least release (about 44%) at after the 8 h study which was comparable to release from the commercial brand tablet, Z. On the other hand, tablets containing HP potato starch prepared by direct compression (Batch P1) exhibited the fastest release (about 79%) at the end of the dissolution study.

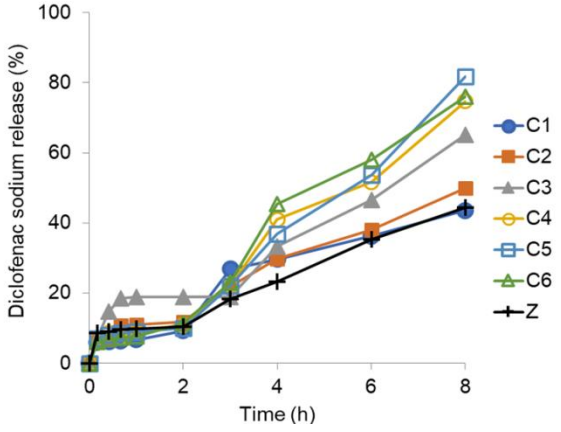

Fig. 2a. Drug release profile of batches of diclofenac sodium tablet formulated with cassava starch (C1-C6) and a commercial tablet brand (Z)

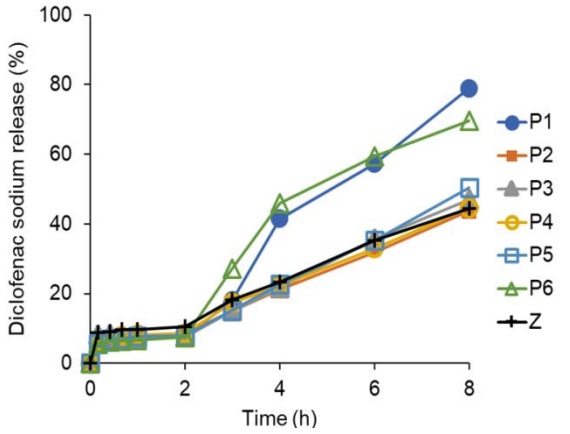

Fig. 2b. Drug release profile of batches of diclofenac sodium tablet formulated with potato starch (P1-P6) and a commercial tablet brand (Z)

Tablets containing HP cassava starch mucilage and prepared by wet granulation were observed to give faster drug release with corresponding increase in concentration of HP mucilage in the order Batch C5 > C4 > C3 > C2. Similar drug release pattern of increased release with increased mucilage concentration was observed from tablets containing HP potato starch mucilage prepared by wet granulation in the order Batch P5 > P4 > P3 > P2. This implies that as the concentration of HP mucilage increased, drug release also increased.

This phenomenon has been documented by Okunlola *et al.* (2017) who investigated HP white yam starch. The rate of drug release was faster from tablets containing HP mucilage than those containing HP powder alone. The process of hydroxypropylation is known to increase hydrophilic hydroxypropyl substitutions which causes loosening of granule bonds resulting in enhanced water influx into the granule structure, rapid rupturing of granule structure and increased granule solubility (Gunaratne and Corke, 2007; Mudiaga-Ojemu *et al.*, 2023). Drug release from tablets containing HP were significantly different ($p < 0.0001$) from those containing the native starches however, there was no significant difference ($p < 0.0001$) in drug release from Batch C1 containing HP cassava starch prepared by direct compression and the commercial brand, Z. Conversely, a significant difference ($p < 0.05$) in drug release was observed from Batch P1 containing HP potato starch prepared by direct compression and the commercial brand, Z but comparable dissolution profile was observed between Batches P5, P4, P3, P2 and the commercial brand, Z. Differences in the release profile of both HP starches can be attributed to the inherent properties of both starches as already documented (Mudiaga-Ojemu *et al.*, 2023).

Table 4. Drug release kinetics and mechanism

Batches	Models					
	Zero order	First order	Higuchi	Hixson-Crowell	Korsmeyer-Peppas	
	r^2	r^2	r^2	r^2	r^2	n
C1	0.9406	0.9590	0.9207	0.9535	0.6256	2.0619
C2	0.9772	0.9803	0.9348	0.9812	0.6256	2.0639
C3	0.9049	0.8958	0.8303	0.9240	0.5134	2.0807
C4	0.9699	0.9266	0.8656	0.9484	0.4700	2.1347
C5	0.9646	0.8774	0.8384	0.9167	0.4095	2.1577
C6	0.9717	0.9486	0.8751	0.9629	0.4870	2.1535
P1	0.9566	0.9120	0.8286	0.9350	0.4308	2.1592
P2	0.9707	0.9593	0.8767	0.9644	0.5547	2.0492
P3	0.9515	0.9408	0.8394	0.9457	0.5152	2.0538
P4	0.9751	0.9672	0.8935	0.9713	0.5739	2.0520
P5	0.9668	0.9442	0.8549	0.9536	0.5116	2.0635
P6	0.9558	0.9641	0.8751	0.9645	0.5255	2.1414
Z	0.9642	0.9643	0.8999	0.9647	0.6013	2.0465

Kinetics and mechanism of drug release

Table 4 shows the kinetics and mechanism of drug release from all the formulated tablets and the commercial brand, Z. Goodness of fit for drug release as extrapolated from correlation co-efficient of the models correlated more with the Zero order for all the tablets containing HP potato starch (Batches P1, P2, P3, P4 and P5) and some Batches C4, C5 and C6 containing HP cassava starch. Zero order indicates that drug release is constant and independent of time

and initial or existing concentration. It shows drug delivery occurs at a constant rate leading to more predictable bioavailability (Turner *et al.*, 2004). Drug release from C2, C3, P6 and Z suited the Hixson-Crowell model indicating drug release is a result of change in surface area and diameter of particles. Release from Batch C1 on the other hand was best described by the First order model where drug release was proportional to the residual amount of drug in the tablets. The kinetics of release varied across the types of HP starches and method of tablet formulation.

Mechanism of drug release as determined by Korsmeyer-Peppas shows drug release from all the batches was swelling-controlled as evidenced by n values ≥ 0.89 i.e super case II transport (Korsmeyer *et al.*, 1983). This implies that swelling of the tablets during dissolution lead to relaxation of starch granule bonds resulting in subsequent drug release.

CONCLUSION

In this study, hydroxypropylated cassava and potato starches produced diclofenac tablet formulations with varying mechanical and release properties. Incorporation of dry powder hydroxypropylated starches produced weak tablets while incorporation of hydroxypropylated cassava starch mucilage produced stronger tablets than hydroxypropylated potato starch. Hydroxypropylated cassava starch incorporated as dry powder by direct compression produced tablets which exhibited more drug retarding characteristics than the corresponding tablets containing hydroxypropylated cassava starch mucilage and its release profile was comparable to that of the commercial tablet. On the other hand, incorporation of the least concentration of hydroxypropylated potato starch mucilage (5.0 %w/v) sustained the release of diclofenac in a manner comparable to the commercial brand. Hydroxypropylated cassava and potato starches whether in their powder or mucilage forms were capable of sustaining the release of diclofenac sodium in tablet formulations.

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