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Evaluation of hydroxypropylated starches as excipients in diclofenac sodium tablet formulations

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Background

- Recent studies are focused on innovative ways to use biomaterials as pharmaceutical excipients.
- Starch is commonly adopted by virtue of being inert, biodegradable, cost effective and biocompatible, etc.
- Starches from maize, wheat, potatoes and cassava are predominantly used in pharmacy.
- Modifications improve starch properties such as stability, heat resistance, water holding capacity, etc [1,2].
- Hydroxypropylation (HP) involves substituting the hydroxyl component of starch with hydroxypropyl moiety [3].
- HP improves thermal characteristics, enzymatic digestibility, etc.
- The HP products have frequently been adopted as stabilizers, emulsifiers, and binders, etc [4].
- The local and abundant availability of starches and its use as an excipient already make it a viable candidate for modification.
- The development of modified starches as drug release retardant excipient is expected to be beneficial to local drug manufacturing

Aim

The aim of the study was to evaluate the excipient potential of hydroxypropylated cassava and potato starches as drug release retardant in diclofenac sodium tablet formulations.

Methods

- Hydroxypropylation of cassava and potato native starches
- Physicochemical characterization of starches; *organoleptics, starch powder flow properties, solubility, volume of sedimentation, water retention capacity, moisture sorption, freeze-thaw stability (syneresis)*.
- High resolution analysis of starches; *Differential scanning calorimetry (DSC), Fourier transform infrared spectroscopy (FTIR), Scanning electron microscopy (SEM)*.
- Preparation of granules and tablets; A total of twelve (12) batches of diclofenac sodium granules and tablets were prepared by wet granulation (Table 1)
- Evaluation of granules and tablets
- *In vitro* drug release studies
- Drug-excipient interaction studies
- Statistical analysis

Table 1: Composition of diclofenac granules and tablets

	Batches	Ingredients (mg)				
		Diclofenac sodium	HP Starch mucilage	HP Starch powder	Native starch mucilage	Native starc powder
Cassava	C1	100	0 [0%]	200	-	-
	C2	100	50 [25%]	150	-	-
	C3	100	100 [50%]	100	-	-
	C4	100	150 [75%]	50	-	-
	C5	100	200 [100%]	-	-	-
	C6	100	-	-	100 [50%]	100
Potato	P1	100	0 [0%]	200	-	-
	P2	100	50 [25%]	150	-	-
	P3	100	100 [50%]	100	-	-
	P4	100	150 [75%]	50	-	-
	P5	100	200 [100%]	-	-	-
	P6	100	-	-	100 [50%]	100

Results

Table 2: Some physicochemical parameters of the starches

Starches	Solubility (%)	Volume of sedimentation (%)	Water retention capacity (g/g)	Moisture sorption		Syneresis (%)
				100% RH	20% RH	
Native cassava	0.21 ± 0.02	50.00 ± 2.00	6.6067 ± 0.9874	56.70 ± 1.41	40.60 ± 2.12	23.64 ± 5.63
HP-cassava	79.40 ± 1.01	35.00 ± 1.00	1.7133 ± 0.9572	83.20 ± 4.81	40.15 ± 0.92	4.16 ± 2.34
Native potato	0.20 ± 0.00	31.33 ± 1.15	4.9267 ± 1.1455	30.85 ± 2.33	12.30 ± 2.55	34.64 ± 2.51
HP-potato	14.20 ± 0.82	29.33 ± 0.58	5.9867 ± 2.2646	188.00 ± 4.67	118.00 ± 0.42	1.08 ± 0.96
p-value	< 0.0001	< 0.0001	0.0135	< 0.0001	< 0.0001	< 0.0001

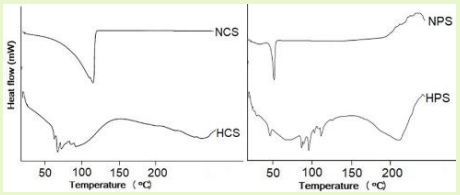

Figure 1: DSC thermogram of native (cassava (NCS) and potato (NPS)) and hydroxypropylated (cassava (HCS) and potato (HPS)) starches

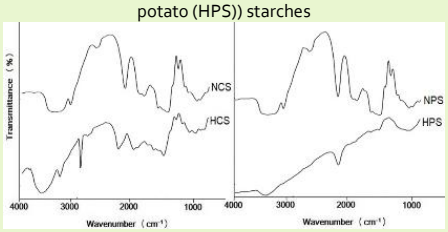

Figure 2: FTIR spectra of native (cassava (NCS) and potato (NPS)) and hydroxypropylated (cassava (HCS) and potato (HPS)) starches

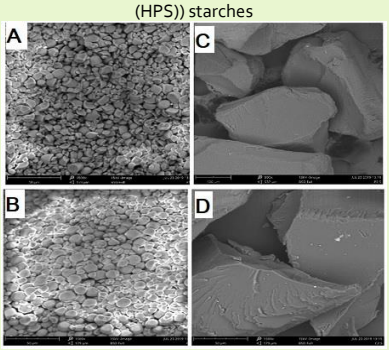

Figure 3: SEM micrograph of native cassava (A) and potato (B)) and hydroxypropylated cassava (C) and potato (D)) starches (1500x)

Table 3: Post compression parameters of diclofenac tablets

Batches	Weight uniformity (g)	Hardness (KPa)	Friability (%)
C1	298.60 ± 1.76	3.60 ± 0.46	9.9976 ± 0.196
C2	298.60 ± 1.84	8.63 ± 0.55	0.3002 ± 0.047
C3	297.13 ± 2.33	10.73 ± 1.10	0.5012 ± 0.047
C4	301.27 ± 2.89	10.63 ± 0.38	0.000 ± 0.000
C5	298.73 ± 1.49	9.93 ± 0.38	0.2997 ± 0.047
C6	299.73 ± 3.33	Exceeded limit	0.3316 ± 0.093
P1	301.33 ± 4.42	3.33 ± 0.58	11.389 ± 0.183
P2	300.20 ± 2.21	6.57 ± 0.60	0.7897 ± 0.003
P3	299.27 ± 2.40	8.27 ± 1.02	0.3988 ± 0.001
P4	300.47 ± 1.92	8.67 ± 0.29	0.3970 ± 0.001
P5	299.47 ± 3.00	7.17 ± 0.29	0.4977 ± 0.046
P6	299.60 ± 2.53	Exceeded limit	0.2665 ± 0.094
p-value	0.1101	< 0.0001	< 0.0001
n	20	10	10

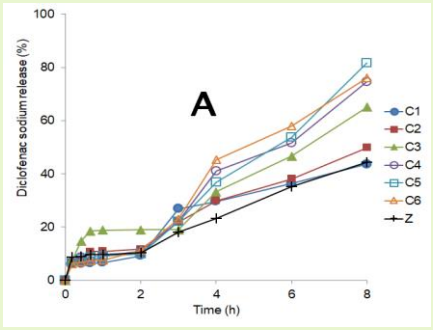

Figure 4: Dissolution profile of formulated tablets with cassava (A) starches

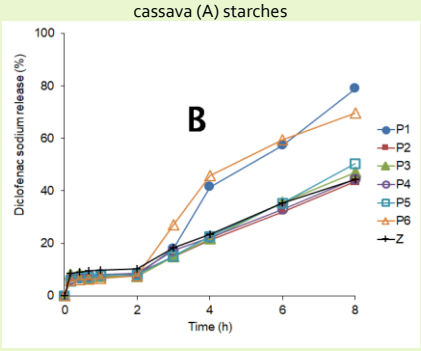

Figure 5: Dissolution profile of formulated tablets with potato (B) starches

Table 4: Drug Release Kinetics and mechanism

Batches	Models					
	Zero	First	Higuchi	Hixson Crowell	Korsmeyer-Peppas	
	R^2	R^2	R^2	R^2	R^2	n
C1	0.9151	0.9590	0.9207	0.9535	0.6256	2.0619
C2	0.9392	0.9803	0.9348	0.9812	0.6256	2.0639
C3	0.8518	0.8958	0.8303	0.9240	0.5134	2.0807
C4	0.9693	0.9266	0.8656	0.9484	0.4700	2.1347
C5	0.9647	0.8774	0.8384	0.9167	0.4095	2.1577
C6	0.9717	0.9486	0.8751	0.9629	0.4870	2.1535
P1	0.9551	0.9120	0.8286	0.9350	0.4308	2.1592
P2	0.9523	0.9593	0.8767	0.9644	0.5547	2.0492
P3	0.9383	0.9408	0.8394	0.9457	0.5152	2.0538
P4	0.9541	0.9672	0.8935	0.9713	0.5739	2.0520
P5	0.9621	0.9442	0.8549	0.9536	0.5116	2.0635
P6	0.9558	0.9641	0.8751	0.9645	0.5255	2.1414
Z	0.9061	0.9643	0.8999	0.9647	0.6013	2.0465

Conclusions

- Hydroxypropylation reduced the volume of sedimentation and improved the solubility and freeze-thaw stability of both starch.
- Hydroxypropylation increased the water retention capacity and moisture sorption of potato starch.
- The tablets batches with HP-starches exhibited drug retarding properties with <50% drug release in 8 h.
- The hydroxyropylated starch batches demonstrated a first order release kinetics and the mechanism of release was through erosion.

References

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