GSC Biological and Pharmaceutical Sciences

eISSN: 2581-3250 CODEN (USA): GBPSC2

Cross Ref DOI: 10.30574/gscbps

Journal homepage: https://gsconlinepress.com/journals/gscbps/

(RESEARCH ARTICLE)

Check for updates

Investigating *Corchorus olitorius* hydrocolloid as a novel matrix former in sustained release delivery of ibuprofen tablet

Akpabio EI *, Effiong DE, Uwah TO and Udoh IF

Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, University of Uyo, Nigeria.

GSC Biological and Pharmaceutical Sciences, 2023, 24(01), 001–010

Publication history: Received on 07 May 2023; revised on 27 June 2023; accepted on 29 June 2023

Article DOI: https://doi.org/10.30574/gscbps.2023.24.1.0241

Abstract

Corchorus olitorius gum in the native form has been researched for use in the food and pharmaceutical industry as a viscosity modifier and binder in immediate release oral tablets. This work sought to investigate the gum as matrix former in the sustained release delivery of Ibuprofen.

Corchorus gum was cold-extracted from the leafy plant part, dried and solid state characterization carried out. Tablets of ibuprofen were prepared using 20% of the gum as matrix former employing the wet granulation technique. Mechanical properties and the release kinetics, using dissolution studies, of the ibuprofen tablets were investigated. Obtained results were compared with those of tablets made with same concentration of a natural gum (Xanthan) and a synthetic one, Hydroxypropylmethylcellulose (HPMC) respectively.

Corchurus gum sustained the release of the drug for up to 8 hours, controlling a constant release at 20% in a sustained release formulation for from half hour to the four and a half hour duration. It also had a better swelling index than Xathan gum and hydroxypropylmethylcellulose (HPMC).Also tablets formulated had good physicomechanical properties that will make the native gum a good choice for use as a sustained release excipient

Keywords: Corchorus gum; Ibuprofen; Sustained Release; Matrix Tablet; Release Kinetics

1. Introduction

Hydrocolloids and biopolymers in their natural or modified forms are finding renewed application in novel drug delivery systems. Like other additives, the amount of hydrocolloids and biopolymers used by formulation scientists in delivery systems vary depending on the desired functionality to be achieved whether in binding, mucoadhesion, disintegration, thickening, or release-retardation [1]. Other such hydrocolloids and biopolymers are employed as co-polymers, suspenders, or even as matrix-formers [1-4]. Particularly, as natural polymers, their versatility and safety, desirable properties such as ready availability and positive impact on manufacturing properties makes them preferred [5-6].

Gums are hydrocolloids and, as matrix-formers, have been specifically useful to restrain, control or moderate the uninhibited drug release that is common with conventional immediate-release solid dosage forms. These are in addition to their imparting compaction and mechanical properties to tablets made from them, through the intra and inter particulate bonding of the hydrocolloids with the drugs [7].

Corchorus olitorius gum is a good example of a hydrocolloid and biopolymer. It is obtained from the leaves of the plant *Corchorus olitorius* (Malvaceae). This plant is found either in the wild or is cultivated as vegetables in parts of Africa and

* Corresponding author: Akpabio EI; Email: pharmeka200@gmail.com

Asia where it is used for food e.g., soup [8]. Several parts and extracts from *Corchorus olitorius* plant have been reported for their medicinal value in treating conditions such as bacterial infections (gonorrhea), gastroenteric symptoms (as purgative) and even in the management of some forms of cancer growth [9]. The gum from Corchorus has been reported to improve the viscosity of starch pastes as well as used as binders for conventional immediate release tablets [8-11].

In this work, Corchorus gum was investigated as a matrix-former for the modified release of ibuprofen oral tablet. Such delivery of the drug would prevent dose dumping or multiple dose administration which could promote pronounced adverse effect or discourage adherence respectively. In so doing, this work will also compare the functionality of Corchorus gum with Xanthan gum (a natural gum) and hydroxy propyl methyl cellulose (HPMC, a synthetic polymer) in sustained release delivery strategy.

2. Materials and method

Ibuprofen powder was bought from (Pauco Pharmaceutical Industry Nig. Ltd), hydroxypropyl methyl cellulose (William Ranson & Son Limited Hitchin), Xanthan gum, *Corchorus olitorius* leaves, magnesium stearate, microcrystalline cellulose and talc (Shermen Chem. Ltd, Sunderland and Sandy, England).

2.1. Preparation of *Corchorus olitorius* gum

The fresh leaves of *Corchorus olitorius* plant were collected and identified at the Department of Pharmacognosy and Natural medicine, Faculty of Pharmacy, University of Uyo, Nigeria in August, 2019. The leaves were chopped into smaller sizes, air-dried at room temperature and weighed.

About 500 g of weighed dried leaves was macerated in 10 L of cold water. The mixture was stirred continuously and thereafter filtered. To the filtrate, equal volume of the mixture of acetone and ethanol (1:1) was added to precipitate the gum. The obtained gum was then washed with acetone repeatedly to remove any chlorophyll left and then dried in the laboratory oven (Techmel Techmel, USA) at 50^{o}C. Dried gum was stored for subsequent evaluation.

2.2. Physicochemical properties of *Corchorus olitorius* gum

The preliminary and confirmatory tests for the gum were carried out using the Molisch and Ruthenium tests respectively. Swelling study, pH determination using pH meter (Thermo scientific Orion Versa Star) and gum solubility in water, ethanol and acetone were carried out using established methods [3].

2.3. Preparation of Granules

The granules were prepared by non-aqueous wet granulation. Three batches of granules were prepared, a polymer for each batch, using the composition as found in table 2. A 95% ethanol was used for the granulation for each batch of granules. The wet masses were passed through a 2mm stainless steel sieve and dried at 60°C for 2 hours in a laboratory hot air oven (P Selecta, Spain). The dried granules were screened using a 1mm sieve to obtain finer granules of uniform size.

Table 1 Composition of each ibuprofen tablet

INGREDIENTS	BATCH I	BATCH II	BATCH III
Ibuprofen (mg)	200	200	200
HPMC (%$^{w}/_{w}$)	20	-	-
Xanthan gum (%$^{w}/_{w}$)	-	20	-
Corchorus olitorius gum (%$^{w}/_{w}$)	-	-	20
Talc (%$^{w}/_{w}$)	1	1	1
Magnesium Stearate (%$^{w}/_{w}$)	1	1	1
MCC qs to (mg)	400	400	400

Key: %$^{w}/_{w}$ as indicated is for the total weight of tablet

2.4. Micromeritics and Compressional properties of granules

2.4.1. Densities, flow rate and angle of repose

The densities, flow rate and angle of repose were carried out in line with our previous works [2, 12] about 20g of the dried granules was weighed into 100ml dry measuring cylinder. The volume was noted as bulk volume (Vb). The cylinder was then tapped until no further reduction in the volume of the granule was observed. The new volume was the tapped volume (Vt). The densities of the granule were calculated using the equations:

$$Bulk\ density\ (Bd) = \frac{W}{Vb} \quad - \quad - \quad (1)$$

$$Tapped\ density\ (Td) = \frac{W}{Vt} \quad - \quad - \quad - (2)$$

Where w is the weight of granule

The granule density was done using fluid displacement method in a pycnometer. After weighing an empty 25 mL pycnometer, it was filled with xylene and re-weighed (W_1). 0.5g of granule (Ws) was transferred into the pycnometer bottle and filled up with xylene but the excess xylene properly cleaned and the bottle was weighed again (W_2). The granule density was then calculated using the equation:

$$\text{Granule density (G d)} = \frac{\rho(W_s)}{W_s-(W_2-W_1)} \quad - \quad - \quad - \quad - \quad (3)$$

Where

ρ is the density of xylene , W_1 is the weight of pycnometer + xylene, W_2 is weight of pycnometer +xylene+ granule sample and Ws is the weight of granule sample.

2.4.2. Hausner's Ratio and Carr's compressibility index

The Hausner's ratio was calculated as the ratio of the tapped density to the bulk density of each batch of granules.

$$Hausner's\ ratio\ (HR) = \frac{T\,d}{B\,d} \quad - \quad - \quad (3)$$

While the Carr's index is determined using the equation

$$Carr's\ index\ (CI) = \frac{T\,d-B\,d}{T\,d} \times 100 \quad - \quad - \quad (4)$$

The flow rate and the angle of repose of the granules was determined using the fixed funnel method. The time taken (t) for 20g (W) of weighed granules to flow through a funnel suspended on a retort stand at a height of 4mm was flow time and the rate was calculated from the equation below;

$$Flow\ rate\ (FR) = \frac{W}{t} \quad - \quad - \quad - \quad - \quad (5)$$

The angle of repose was determined from the granule heap formed flowing freely from the fixed funnel onto a flat horizontal surface. The values of height of heap (h) formed and that of the diameter (d) of the cone base were measured respectively using a ruler. Angle of repose was calculated using the equation below:

$$\theta = \tan^{-1}\left(\frac{2h}{d}\right) \quad - \quad - \quad - \quad - \quad - \quad (6)$$

2.5. Packing Fraction and Granule Porosity of granules

The packing fraction of the different batches of granules was determined using the equation.

$$\text{Packing Fraction} = \frac{B\,d}{G\,d} \quad - \quad - \quad - \quad - \quad (8)$$

The porosity of each batch of granules was determined using the equation:

$$Granule\ Porosity = (1 - \frac{\mathrm{B\ d}}{\mathrm{G\ d}}) \times 100 \quad - - - \quad (9)$$

2.6. Preparation of Ibuprofen Tablets

The prepared granules were lubricated with 1%w/w each of talc and magnesium stearate, then compressed into tablets using a single punch tableting press (Cadmach, Ahmedabab, India) fitted with 12.5mm flat faced punches at a constant compression fore of 15 KN.

2.7. Properties of the Tablets

2.7.1. Weight Uniformity Test

Twenty tablets were randomly selected from each batch and weighed individually using an electronic balance (OHAUS, Galaxy). The mean deviation and coefficient of variation were calculated.

2.7.2. Tablet dimensions

This was done using ten tablets which were randomly selected from each batch. The thickness and diameter of each tablet was determined using the micrometer screw gauge (KFW Scientific Industries Ambala Cantt India).

2.7.3. Tablet Porosity

The tablet porosity was calculated using the formula;

$$Tablet\ porosity = 100\left[1 - \frac{4w}{\rho\pi \mathrm{d}^2 \mathrm{h}}\right] \quad - - - - \quad (10)$$

Where;

m = mean weight of tablets, ρ = particle density, d = mean tablet diameter

h = tablet thickness

2.7.4. Mechanical properties of tablet

The crushing strength of ten tablets from each batch randomly selected was determined using Mosanto hardness tester (Rolex, Chandigarh).

The friability of 5 tablets was carried out using the Roche fribrillator (UNID 056830 Campbell electronic, Mumbai, India). The five selected tablets from each batch were dusted, weighed (w_0) and placed in the Roche fribillator operated at a speed of 25 revolutions per minute for 4 minutes. The tablets were then removed, dusted and weighed again (w_1). The friability was then calculated using the equation below:

$$\text{Friability} = \frac{W_0 - W_1}{W_1} \times 100 \quad - - - \quad (11)$$

2.7.5. Swelling Study

The swelling index was carried out over a period of time (8 hours). Three tablets from each batch were weighed (w_0) prior to placement in a petri dish containing 0.1N HCl. The tablets were taken out from the petri dish every 30 minutes and weighed (w_1) after mopping off the fluid medium from the swollen tablets. The swelling index of the tablet was then determined using the equation.

$$SI = \frac{W_1 - W_0}{W_0} \times 100 \quad - - - - \quad (12)$$

2.8. In Vitro Drug Release Study of the Ibuprofen Tablet

In vitro dissolution study for the tablets was carried out using the USP basket dissolution method agitation set at 50 revolutions per minute in 900 mL medium of distilled water maintained at 37 ± 0.5°C. A 10 mL aliquot of the dissolution medium was withdrawn at interval of 30 minutes filtered through a Whatmann filter paper and assayed using the UV

spectrophotometer at a wave length of 264 nm. An equal volume of fresh medium was replaced into the dissolution medium after sampling so as to maintain the constant volume throughout the test. The test lasted for eight (8) hours.

2.8.1. Preparation of Ibuprofen Standard Calibration Curve

The standard concentration was prepared by dissolving 10 mg of pure ibuprofen powder in 10 mL of distilled water. This stock concentration was serially diluted using distilled water. The drug was assayed using the spectrophotometer to note the absorbance of the different concentration, then a standard curve of absorbance versus concentration was plotted.

2.8.2. Absolute Drug Content of Ibuprofen Tablets

Ten tablets from each batch was crushed and powdered. Exactly weighed out was crushed powder equivalent to 200mg of ibuprofen and dissolved in 100 mL of 0.1N HCl. 0.1 mL of the filtrate was diluted to 10 mL with 0.1N HCl and the drug content determined at a wavelength of 264nm.

2.8.3. Kinetic Release Models of Ibuprofen Sustained Release Tablets.

- **Zero order- kinetic model;** cumulative amount of drug released versus time.
- **First order kinetic model;** log cumulative % drug remaining versus time.
- **Higuchi model;** cumulative % drug released versus square root of time.

The model with the highest correlation coefficient (R^2) was considered to be the best fit for the designated kinetic release.

2.8.4. Mechanism of Drug Release from Ibuprofen Sustained Release Matrix Tablets

The mechanism of drug release was determined by plotting the percentage drug release fitted into Korsemeyer-Peppas model equation.

Korsemeyer-Peppas model; log cumulative % drug released versus log time with the value of the slope indicating the mechanism of drug release followed by the matrix.

3. Result and discussion

3.1. Properties of Corchorus olitorius gum

The leaves of *Corchorus olitorius* plant gave 2.04% w/w gum. The organoleptic properties showed that the extracted gum from the plant is dark brown with a characteristic odour as opposed to the Xanthan gum which is off-white colour. The part of the plant where the gum is obtained can affect its colour depending on the quantity of the polymer or secondary metabolite present. The pH of xanthan gum is neutral while that of *Corchorus olitorius* is slightly alkaline. Tables 2 and 3 below show some of the properties of the gums.

Table 2 Properties of gums of Xanthan gum and *Corchorus olitorius*

Parameters	**Xanthan Gum**	**Corchorus olitorius**
Colour and Odour	Cream coloured powder with no particular odour	Dark brown with a characteristic odour
pH 1% solution	7.30±0.01	7.90±0.01
Swelling index	7.20±0.01	8.10±0.01
Solubility		
In water with Agitation	Soluble	Soluble, forming a mucilaginous gel
In ethanol with Agitation	Insoluble	Insoluble
In acetone with Agitation	Insoluble	Insoluble

The gums are soluble in water but insoluble in both ethanol and acetone. High water solubility of a pharmaceutical excipient imparts mouth feel of formulation as it mixes with saliva, propensity to hold flavor and moisture in liquid formulations, provide elasticity and possess freeze thaw ability [13].

Table 3 Confirmatory tests of the gums

S/N	Test	Observation	Inference
1	**Ruthenium Test**		
	Small quantity of dried gum powder mounted on a slide with ruthenium red solution and observed under a microscope	Pink colour develops in both samples	Gum present
2	**Molisch Test**		
	0.1g of dried gum powder + Molisch's reagent + concentrated H_2SO_4 on the side of the test tube	Violet colour observed at the two layers in both samples	Carbohydrate present

The treatment of both gums with ruthenium red and Molisch test gave results indicating they are gums and contained carbohydrate as shown in Table 3 above.

3.2. Properties of the prepared granules

The colour of the *Corchorus olitorius* gum imparted on the granules and tablets formulated with it. The micromeritics of the granules and the mechanical properties of the tablets formed from the gums are presented in tables 4 and 5 respectively

Table 4 Micromeritics of Granules

Parameters	Batch I	Batch II	Batch III
Bulk density (g/mL)	0.24 ± 0.01	0.32 ± 0.01	0.34 ± 0.01
Tapped density (g/mL)	0.33 ± 0.02	0.41 ± 0.03	0.43 ± 0.03
Hausner's ratio	1.38 ± 0.05	1.28 ± 0.04	1.26 ± 0.04
Carr's index (%)	27.27 ± 0.01	21.95 ± 0.01	20.93 ± 0.01
Flow rate (g/s)	2.86 ± 0.10	4.65 ± 0.20	4.55 ± 0.20
Angle of repose (^{o})	31 ± 0.90	26.57± 0.80	25.64 ± 0.70
Granule density	1.02	1.13	1.23
Packing fraction	0.24	0.28	0.27
Granule porosity	76%	72%	73%

Key: Batch I: formulation with HPMC as matrix former, Batch II: formulation with Xanthan gum as matrix former, Batch III is formulation with Corchorus gum as the matrix former.

The flow properties of the granules show that granules of *Corchorus* and Xanthan gum were had significantly higher and better flow rates and granule densities than granules from HPMC (Table 4). This is also seen in the granule porosity which is a function of granule density and shape. Since the granules were made from the same equipment and procedures the difference in the porosity will be mainly from the granule density which is directly related to the true density of the individual gums. Although all tablet formulations passed the weakness test of friability falling within permissible values of ≤ 1%. None of the tablet formulations exceeded the 1 % mark. Friability depicts tablet deformation that could occur resulting from the tablet morphology as rougher tablet surfaces are more friable. Hence the formulated tablets possessed good morphology. The tablets formed with *Corchorus* gum had higher mechanical than those of HPMC

and Xanthan gums and can be ranked in terms of tensile strength as Batch III> Batch I> Batch II as well as in hardness Batch III>BatchI>Batch II. However as regards the compact density, the tablets are ranked Batch II> Batch III > Batch I

Tablet porosity was obtained as 59%, 54% and 52% for batches I, II and III respectively. As a good predictor of how liquids (eg dissolution fluids) find their way into tablet matrix to initiate disintegration or dissolution, porosity also influences drug dissolution rate and solubility, surface area, particle size and polymer type [14]. There was also a significant statistical difference ($p<0.05$) in the granule density, granule porosity, packing fraction and tablet porosity following the use of the different polymers ranging from HPMC to Xanthan gum to Corchorus gum.

The drug content for batch I, II and III was obtained as 99.58%, 90.1% and 103.73% respectively. The content of tablets from the three formulations fulfills the standard by official compendia of 85% to 115%

Table 5 Physical Properties of Ibuprofen Tablets

Parameters	**Batch I**	**Batch II**	**Batch III**
Weight uniformity (g); n=20	0.37 ± 0.01	0.41 ± 0.01	0.39 ± 0.01
Hardness (KgF); n=10	5.36 ± 1.16	5.00 ± 1.12	6.32 ± 1.00
Tablet diameter (mm); n=10	12.56 ± 0.02	12.52 ± 0.02	12.53 ± 0.02
Tablet thickness (mm); n=10	2.70 ± 0.06	2.66 ± 0.07	2.63 ± 0.08
Friability (%)	0.60	0.59	0.67
Tablet porosity (%)	7.13 ± 3.36	9.29 ± 4.22	5.85 ± 3.62
Tensile strength (MNm^{-2})	0.10 ± 0.02	0.09 ± 0.02	0.12 ± 0.02
Compact density (g/mL)	1.09 ± 0.03	1.23 ± 0.05	1.21 ± 0.07

Key: Batch I: formulation with HPMC as matrix former, Batch II: formulation with Xanthan gum as matrix former, Batch III is formulation with Corchorus gum as the matrix former.

The drug release profile of the 3 different formulations is presented in figure 2 and 3 while the kinetics parameters are presented in table 6. All the formulations sustained release for the 8 hour duration, releasing only about 20% of its drug content between the half hour and the four and half hour time after which time the percentage release started rising. Drug release kinetics from a matrix formulation is generally affected by polymer type, concentration or the properties of the drug formulated [15]. Thus the drug dissolution, swelling property of the polymer in the matrix as well as its viscosity on swelling will control the rate at which the drug moves out of the swollen matrix former [15-17]. This may explain why the tablet formulation with *corchorus* gum sustained the release longer. The tablet formulations followed the zero order kinetics, showing the highest R^2 value for zero order release. This implies that the amount of drug release from the matrix in a dissolution medium is constant irrespective of the amount of the drug that remains in the formulation. Sustained release tablets or the controlled drug release formulation have been reported to follow zero order kinetics as seen in delivery of theophylline using carbopol [15].

The mechanism of the drug release of the formulation reveals that it follows the anomalous (non-Fikian) diffusion where the exponent of time in the Korsemeyer Peppas' equation (n) is $0.5<n<1$. This implies that drug release is dependent on the polymer relaxation that will thus allow the out movement of the dissolved drug molecules.

Table 6 Release kinetics constants using different models

	R^2				
Batches	**Zero order**	**Higuchi**	**First order**	**Korsemeyer-Peppas**	**Diffusion exponent (n)**
BI	**0.8795**	0.7523	0.6856	0.7185	0.5495
BII	**0.8928**	0.7768	0.5556	0.7059	0.5748
BIII	**0.8917**	0.7778	0.6684	0.7095	0.566

Key: Batch I: formulation with HPMC as matrix former, Batch II: formulation with Xanthan gum as matrix former, Batch III is formulation with *Corchorus* gum as the matrix former.

The swelling studies measures how well molecules of the formulation (the tablet formulated with the different types of polymers) absorbs water molecules and increase in size on being wet. The result shows that batch III tablets (containing gum of *Corchorus olitorius*) exhibited the highest swelling index followed by Batch I tablets (HPMC) then Batch II (Xanthan gum). Swelling increased with longer contact time with the dissolution medium. The type of polymer (matrix former) use however did not significantly affect the swelling index ($p>0.05$). A good swelling or hydration capacity of a formulation may regulate drug release from matrix systems and *C. Olitorious* could be employed as matrix former for sustained release drug formulation [17, 18]

The time taken to release 50% and 90% respectively (t_{50} and t_{90}) of the drugs from the respective formulations is presented in table 7. Generally, it took a longer time (around 5 hours) for the first 50% of the drug to be released, but the remaining 40% (between T_{50} and T_{90}) was released at a shorter time of less than half of the previous time. While the T_{90} of these formulations are similar to those of our earlier work with the same drug compact but using Carbopol 940 as the matrix former, the T_{50} was far longer in the present formulations unlike that of Carbopol 940 that was ashorter time of about 3hours [19].

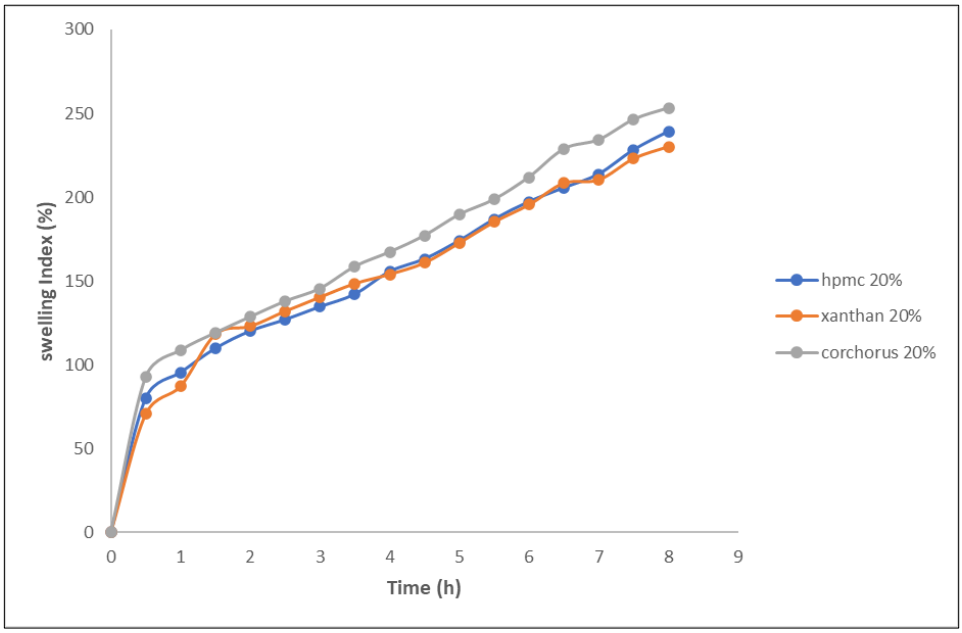

Figure 1 Swelling studies of the formulated tablets of different polymers in 0.1 HCl

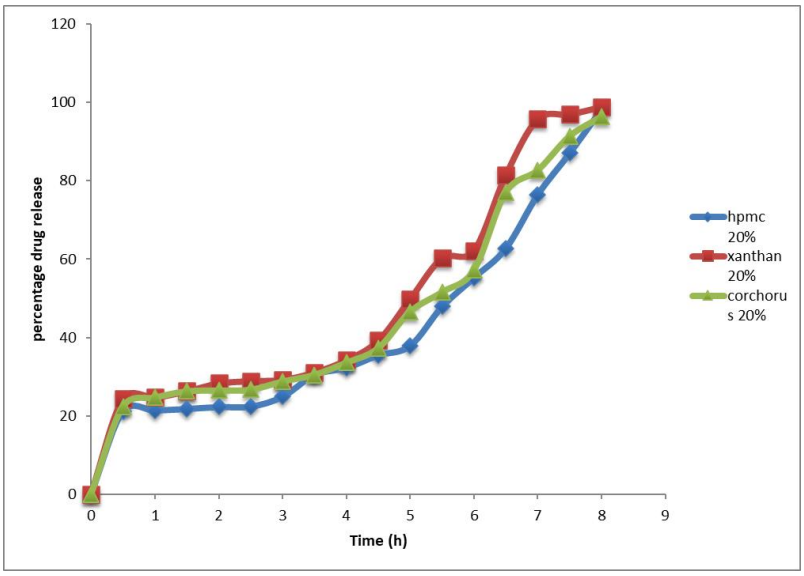

Figure 2 Release profile of ibuprofen matrix tablet using the different polymers

Table 7 Release kinetics parameters of the drug from the different formulations

Kinetic parameter	Batch I	Batch II	Batch III
T_{50} (hr)	5.6	5	5.3
T_{90} (hr)	7.7	6.8	7.4

Key: Batch I: formulation with HPMC as matrix former, Batch II: formulation with Xanthan gum as matrix former, Batch III is formulation with Corchorus gum as the matrix former.

4. Conclusion

Corchorus olitorius leaves gum retarded the release of the drug ibuprofen for 8 hours. From the dissolution profile, the controlled release duration was maintained within the 1 hour and 5-hour mark. Beyond its colour the properties of the native gum compared favourably well with xanthan gum without needing any adjustment or modification. This study thus showed the use of corchorus as a matrix former for sustaining or in the controlled release of ibuprofen.

Compliance with ethical standards

Acknowledgments

The authors would like to acknowledge the assistance in the laboratory by Mr Emma Uduk of the Department of Pharmaceutics and Pharmaceutical Technology, University of Uyo,

Disclosure of conflict of interest

The authors declare no conflict of interest.

References

[1] Ayorinde J O, Itiola O A, Odeku, O A, Odeniyi M A. Influence of binder type and process parameters on the compression properties and microbial survival in diclofenac tablet formulations. Brazilian Journal of Pharmaceutical Science. 2011; 47(4):845-854.

[2] Odeniyi M A, Babalola A O, Ayorinde J O. Evaluation of Cedrela gum as a binder and bioadhesive component in ibuprofen tablet formulations. Brazilian Journal of Pharmaceutical Sciences. 2013;49(1):95-105

[3] Akpabio E I, Uwah T O, Effiong, D E, Godwin, J. Evaluating Hydrocolloids of Sida acuta as Sustained Release Matrix for Ibuprofen Tablet. Global Journals of Medical Research. 2020; 20 (4):15-21

[4] Odeku O A, Okunlola A, Lamprecht A. Formulation and in vitro evaluation of natural gum-based microbeads for delivery of Ibuprofen. Tropical Journal of Pharmaceutical Research. 2014; 13 (10):1577-1583

[5] Uwah T O, Akpabio E I, Effiong D E. Plants as pharmaceutical excipients in oral sustained drug delivery systems: A review. Journal of Applied Pharmaceutical Research. 2021; 9(3): 26-38. Available from www.japtronline.com

[6] Manjula B S, Srinatha A, and Sridhar B K. Evaluation of Hydrophilic Polymers and Their Combinations in Formulation of Sustained Release Matrix Tablets of Water Soluble Drug. Indian Journal of Pharmaceutical Education and Research. 2014; 48(3): 48- 59.

[7] Joneja S K, Harkum W W, Skimmer P E, Guo J H. Investigating the fundamental effects of binders on pharmaceutical tablet performance. Drug Development and Industrial Pharmacy. 1999; 251(10):29-35.

[8] Ordu J I, Abidde T O, and Okafo S E. Evaluation of the binding properties of gum obtained from dried leaves of Cochoros olitorious on metronidazole tablets formulation. The Pharma Innovation Journal. 2018; 7(5): 688-694

[9] Kuete V, Karaosmanoğlu O, Sivas H. Anticancer Activities of African Medicinal Spices and Vegetables In: Kuete V(Editor),Medicinal Spices and Vegetables from Africa, Academic Press. 2017; 271-297.

[10] Oladipo F Y, Nwokocha L M. Effect of Sida acuta and Corchorus olitorius mucilages on the physicochemical properties of maize and sorghum starches. Asian Journal of Applied Sciences. 2011; 4 (5):514-525

[11] Osonwa U E, Uronnachi E M, Umeyor C E, Onwuzuligbo C C. Physicotechnical Properties of Paracetamol Tablets Formulated with the Gum from the Fresh Leaves of Corchorus Olitorius. International Journal of Pharmaceutical Science Research. 2012; 3(8): 2676-2679.

[12] Akpabio E I, Ekong U S, Uwah T O, Ekpa E D, Ubulom P M E, Jacobs G E. Formulation and Evaluation of Theophylline Sustained Release Tablet using Lasianthera africana gum. Nigerian Journal of Pharmaceutical and Applied Science Research. 2016; 5 (2): 41-48.

[13] Christopher R, Dupon A. Characterizing Polymeric Excipients. Journal of Drug Delivery and Formulation. 2011; 2: 87 – 91.

[14] Yassin S, Su K, Lin H, Gladden L F, Zeitler J A. Diffusion and swelling measurements in pharmaceutical powder compacts using terahertz pulsed imaging. Journal of pharmaceutical sciences. 2015; 104(5):1658–1667. https://doi.org/10.1002/jps.24376

[15] Lubrizol Life Science Health. Formulating Controlled Release Tablets and Capsules with Carbopol ®* Polymers. Pharmaceutical bulletin. 2011; 31:1-22

[16] Siepmann J, and Siepmann F. Modelling of Diffusion Controlled Drug Delivery, Journal of Controlled Release. 2012;161: 351-362. Available from https://doi.org/10.1016/j.jconrel.2011.10.006

[17] Monday C L, Cook P. Compressed Xanthine and Karaya gum matrices, hydration, erosion and drug release mechanism. International Journal of Pharmaceutical Science. 2000; 1 (2):179 – 192.

[18] Ordu J I, Amarauche C. Natural hydrogel obtained from leaves of *Cochorus olitorious* plant in South-South Nigeria. 1: Preliminary characterization studies. International . Journal of Pharmaceutical Research and Allied Science. 2015; 4(1):1-7

[19] Akpabio E I, Effiong D E, Uwah TO, and Ofoefule S I. Effect of Granules Size on the Release Kinetics of Ibuprofen from Its Matrix Tablet. Open Access Library Journal. 2022; 9: 1-15. Available from https://doi.org/10.4236/oalib.1107920