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Formulation and Evaluation of Sustained-Release Diclofenac Sodium Tablets Using Hydrophilic Polymer Blends

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Keywords: Xanthan gum, a polysaccharide, Crude cashew gum, Diclofenac Sodium powder, Wet Granulation Method

ABSTRACT

The term modified – release dosage form is used to describe products that alter the timing and rate of release of the drug substance. A modified-release dosage form is defined "as one for which the drug release characteristics of time course and/or location are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms such as solutions, ointments, or promptly dissolving dosages forms. Xanthan gum, a polysaccharide, Crude cashew gum, Diclofenac Sodium powder, Hydroxypropyl Methylcellulose, Microcrystalline Cellulose, Talc, and Magnesium stearate. Wet granulation, Procedure of Wet Granulation in 6-Step. All the batches of tablets passed the uniformity of weight test and drug content test the batches of tablets but batch 3 passed the crushing strength test All the batches of tablets but batches 4 and 10 passed the friability test. Tablets containing only xanthan gum as release modifier achieved the highest crushing strength friability ratio (CSFR) with those in batch 10 having the lowest. Tablets in batch 2 had the highest swelling index and those in batch 3 had the lowest swelling index. The study has shown that cashew and xanthan gums used alone cannot efficiently control drug release. Batches 7 and 8 containing xanthan gum and HPMC were able to cause sustained drug release comparable to Voltaren Retard.

INTRODUCTION:

Drug products designed to reduce the frequency of dosing by modifying the rate of drug absorption have been available for many years There is regular and ongoing research into the use of naturally occurring biocompatible polymeric materials in the design of dosage forms for oral controlled release administration. The search for alternative products from renewable sources has increased significantly over the years. Products that can be utilized over a long period will reduce the cost of importing these basic ingredients that are used in the pharmaceutical industry. Normally, plant products serve as a good alternative to synthetic materials because of local accessibility, eco-friendliness, and lower costs compared to imported synthetic products. [1]

Hydrophilic polymers have attracted considerable attention for use as sustained and controlled release devices for the delivery of both water-soluble and water-insoluble agents. Their characteristics and ability to hydrate and form a gel layer are well known and essential to sustain and control drug release from matrices. The hydrated gel layer thickness determines the diffusion path of the drug molecules through the polymer mass into the diffusion medium. Gums are natural exudates from the bark of trees, and they have been of great pharmaceutical importance. Plant polysaccharides are useful for the construction of drug delivery systems for specific drug delivery. Some natural gums e.g. guar, tamarind, locust bean, and okra gums as polymeric materials have been reported to be suitable in the design of controlled drug delivery systems because of their swelling or permeability profiles. [5]

Several approaches have been used to obtain controlled drug release, but the hydrophilic matrix is recognized as the simplest and the most widely used method. Upon ingestion of a hydrophilic matrix tablet, drug release results initially from swelling which causes a gel layer to form on the tablet surface. This gel layer retards further ingress of fluid and subsequent drug release. The swelling of the polymer matrix very often occurs with and both of them contribute to the overall rate of drug release. The use of hydrophilic gum blends as the hydrophilic matrix can further be investigated to determine whether the release of the active ingredient can be controlled further. Several gum blends have been researched into and the use of a blend of xanthan and cashew gums will be investigated.

Hydrophilic polymers are widely used in the formulation of modified-release oral dosage forms. Their convenience and ease of manufacture may cut down the cost of the final product. Besides, the hydrophilic polymer matrix system offers several additional advantages over other technologies for controlled release drug delivery. The mechanism and the influence of various technological and formulation variables on the drug release from hydrophilic systems have been well studied. Until now, a large number of natural and synthetic polymers, single or in combinations, have been listed as hydrophilic matrix excipients. [2]

Introduction of matrix tablet as sustained-release has given a breakthrough for novel drug delivery systems in the field of Pharmaceutical Technology. It excludes complex production procedures such as coating and pelletization during manufacturing and the drug release rate from the dosage form is controlled mainly by the type and proportion of polymer used in the preparations. Because of increased complication and expense involved in the marketing of new drug entities, scientists have focused greater attention on the development of sustained-release or controlled release drug delivery systems.

Sustained Release:- includes any drug delivery system that achieves slow release of the drug over an extended period. Most sustained-release formulations are designed so that the administration of a single dosage unit provides the immediate release of an amount drug that promptly produces the desired therapeutic effect and gradual and continual release of additional amounts of the drug to maintain this level of effect over an extended period usually eight to twelve hours.[21]

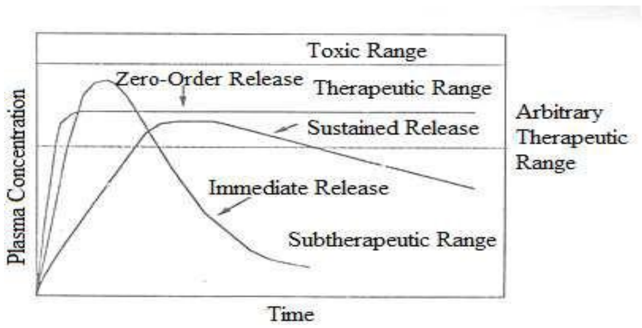

Figure No. 1: Plasma Drug Concentration Profiles for Conventional Tablet Formulation, a Sustained-Release Formulation and a Zero Order Controlled Release Formulation

Controlled and Sustained Release has both been used inconsistently and confusingly. Both represent a separate delivery process. Sustained Release constitutes any dosage form that provides medication over an extended time or denotes that the system can provide some actual therapeutic control whether this is temporal, spatial nature, or both. Sustained Release systems generally do not attain zero-order type release and usually try to mimic zero-order release by providing drugs in a slow first order.[18]

Repeat action tablets are an alternative method of sustained release in which multiple doses of drugs are contained within a dosage form and each dose is released at periodic intervals. Delayed-release system, in contrast, may not be sustained, since often the function of these dosage forms is to maintain the drug in the dosage for some time before release, for example, enteric-coated tablets.

The ideal way of providing an exact amount of drug at the site of action for a precise period is usually approximated by most systems. This approximation is achieved by creating a constant concentration in the body or an organ over an extended time; in other words, the amount of drug entering the system is equivalent to the amount of drug removed from the system. All forms of metabolism and excretion are included in the removal process: urinary excretion, enterohepatic recycling, sweat, fecal, and so on. Since for most of the drugs these elimination processes are first order, it can be said that at a certain blood level, the drug will have a specific rate of elimination. The idea is to deliver the drug at this exact rate for an extended period. This is represented mathematically as follows,[17]

$$\text{Rate in} = \text{Rate out} = k_{elim} \times Cd \times Vd$$

Where Cd is the desired drug level, Vd is the volume of distribution, and k_{elim} is the rate constant of drug elimination from the body. Often such exacting delivery rates prove to be difficult to achieve through administration routes other than intravenous infusion. Non-invasive routes, for example, the oral route is thus preferred.

Advantages of sustained release dosage forms

- **Patient Compliance**
- **Reduced 'see-saw' fluctuation**
- **Reduced total dose**
- **Improved efficiency in treatment:**
- **Economy:**

- **Improved therapy:**

i. Sustained blood level:

ii. Attenuation of adverse effects:

A matrix is defined as a well-mixed composite of one or more drugs with gelling agent i.e. hydrophilic polymers. By the sustained release method, therapeutically effective concentration can be achieved in the systemic circulation over an extended period, thus achieving better compliance of patients. Numerous sustained-release oral dosage forms such as membrane-controlled systems, matrices with water-soluble/insoluble polymers or waxes, and osmotic systems have been developed. Intense research has recently focused on the designation of sustained-release systems for poorly water-soluble drugs. Various drug delivery techniques have been developed to sustain the release of drugs, including triple-layered tablets and osmotic pumps with laser-drilled holes. These technologies are intricate and relatively expensive to manufacture. Thus, there remains an interest in developing novel formulations that allow for sustained release of drugs using readily available, inexpensive excipients.

Xanthan gum is normally used as a food additive and rheology modifier. It is used as a food thickening agent and as a stabilizer. Cashew is readily available in Ghana and the most commonly used part is the nuts that are used as food ingredients, but the gum can be worked on and exploited for use in the pharmaceutical industry. The basic idea behind the use of the matrix system is to maintain a constant level of drug in the blood plasma although the drug does not undergo disintegration. This is very useful when a sustained effect of diclofenac sodium is required for a long time to treat some chronic conditions like rheumatoid arthritis, osteoarthritis, chronic pain, ankylosing spondylitis, and actinic keratosis.[6, 9]

MATERIALS AND METHODS:

MATERIALS:

Xanthan gum, a polysaccharide, derived from the bacterial coat of *Xanthomonas campestris* was obtained from the Chemical Store of the Department of Pharmaceutics, KNUST, Kumasi. Crude cashew gum was obtained from the Wenchi Cashew Plantation as natural exudates from the stem barks of the plant *Anacardium occidentale*, family, Anacardiaceae at Wenchi in the

Brong Ahafo region of Ghana. The plant was authenticated by the curator of the plantation. Other materials used include Diclofenac Sodium powder (Hubei Prosperity Galaxy Chemical Co., Ltd., China), Hydroxypropyl Methylcellulose (UK Chemicals, Kumasi), Microcrystalline Cellulose (Amponsah-Effah Pharmaceuticals Ltd., Kumasi). Talc and Magnesium stearate were obtained from the Chemical Store of the Department of Pharmaceutics, KNUST, Kumasi.[11,20]

CHEMICALS AND REAGENTS:

96 % ethanol, diethyl ether, concentrated hydrochloric acid, distilled water was obtained from the Chemical Store of the Department of Pharmaceutics and the Department of Pharmaceutical Chemistry, Faculty of Pharmacy and Pharmaceutical Sciences, KNUST. Kumasi. Sodium hydroxide pellets, phosphoric acid, sodium dihydrogen phosphate, and disodium hydrogen phosphate were obtained from Lab Chem. Ltd. Kumasi.

EQUIPMENT AND APPARATUS

Eutech pH meter (pH 510, pH/mV/^{0}C meter), porcelain mortar and pestle, Analytical balance (Adam Equipment), UV spectrophotometer (T90 UV/VIS spectrometer, PG Instruments Ltd.), Erweka Dissolution Apparatus, (Type DT 6, GmbH Heusenstamm, Germany), Erweka Friabilator (USP), Brookfield Viscometer (Brookfield Engineering Lab Inc., Middleboro, MA, USA), Number 4 sintered glass filter, Stormer Viscometer, Retsch Laboratory Sieves, Sartorius Electrical Balance, Whatman filter papers, Retsch Mechanical Shaker, desiccator, Monsanto Tablet Hardness Tester, Single Punch Tableting Machine, Electronic Vernier calipers, among others were the equipment and apparatus used.[22, 24]

In addition to the active or therapeutic ingredient, tablets contain some inert materials; these are known as additives or excipients. They may be classified according to the part they play in the finished tablet. The first group contains those which help to impart satisfactory processing and compression characteristics to the formulation. These include diluents, binders, glidants, and lubricants. The second group of added substances helps to give additional desirable physical characteristics to the finished tablet. Included in this group are disintegrants, colors, etc.

DILUENTS

Frequently the single dose of the active ingredient is so small and inert substances are added to increase the bulk to make the tablet a practical size for compression. Diluents used for this purpose include dicalcium phosphate, calcium sulfate, lactose, cellulose, kaolin, manning, dry starch and powdered sugar, microcrystallinecellulose). [19, 15]

BINDERS

These are agents used to impart cohesive qualities to the powdered materials. They impart cohesiveness to the tablet formulation which ensures the tablet remaining intact after compression as well as improving the free-flowing qualities by the formulation of granules of desired hardness and size. Materials commonly used as binders include starch, gelatin, and sugars. Natural and synthetic gums that have been used include acacia, sodium alginate, panwar gum, ghatti gum, carboxymethylcellulose, methylcellulose, and polyvinylpyrrolidone.

The quantity of binder used has considerable influence on the characteristics of the compressed tablet. The use of too much binder or too strong a binder will make a hard tablet that will not disintegrate easily and will cause excessive wear of punches and dies.[10,12]

LUBRICANTS

Lubricants have several functions in tablet manufacture. They prevent adhesion of tablet material to the surface of dies and punches, reduce interparticle friction, facilitate ejection of the tablets from the die cavity, and may improve the rate of flow of the tablet granulation. Commonly used lubricants include talc, magnesium stearate, calcium stearate hydrogenated vegetable oil, and polyethylene glycol. In selecting a lubricant, proper attention must be given to its compatibility with the drug agent.[8,14]

GLIDANTS

A glidant is a substance that improves the flow characteristics of a powder mixture. These materials are normally added in the dry state just before compression. Colloidal silicon dioxide is the most commonly used at usually low concentrations.[5, 13]

DISINTEGRANTS

A disintegrate is a substance or mixture of substances, added to a tablet to facilitate its breakup or disintegration after administration. The active ingredient must be released for the tablet matrix efficiently as possible for its rapid dissolution. Materials serving as disintegrate have been classified chemically as starches, clays, cellulose, algins, gums, and cross-linked polymers. The oldest and still the most popular disintegrate are corn and potato starch which have been well dried and powdered. A group of materials known as super disintegrates has gained popularity as disintegrating agents. The name comes from the low levels at which they are very effective. Examples are croscarmellose and cross povidone. The method of addition of the disintegrate in the course of granulation is also of much importance.[16]

Tablet characteristics

Tablets as a dosage form should meet certain specific requirements. The diameter, shape, thickness, accuracy of dosage, weight, hardness, stability, disintegration time, and dissolution have to conform to certain parameters.

TABLET HARDNESS AND FRIABILITY

The resistance of the tablet to chipping, abrasion, or breakage under conditions of storage, transportation, and handling before usage depends on its hardness. Hardness determinations are made throughout the tablet runs to determine the need for pressure adjustment on the tableting machine. A tablet property related to hardness is friability. This parameter assesses the ability of the tablet to withstand abrasion in packaging, handling, and shipping. [20]

UNIFORMITY OF DOSAGE FORMS

Tablet Weight

The volumetric fill of the die cavity determines the weight of the compressed tablet. The weight of the tablet is the quantity of the granulation which contains the labeled amount of the therapeutic agent. The tablet weights must conform to the set standards as in the USP or BP.

Content Uniformity

Each tablet must contain the intended drug quantity with little variation among the tablets in a batch. The drug quantity per tablet of average weight is determined analytically and compared to standards as set in the monographs.

TABLET DISINTEGRATION

To be absorbed, a drug substance must go into solution, but the disintegration test is a measure only of the time required under a given set of conditions for a group of tablets to disintegrate into particles. It is therefore recognized that the in vitro tablet disintegration test does not necessarily bear a relationship to the in vivo action of the tablet. The maximum disintegration time often set at 15 minutes for ordinary tablets and 60 minutes for coated tablets. This test does not apply to depot tablets, lozenges, and chewable tablets.

DISSOLUTION

For certain tablets, monographs specify compliance with limits on dissolution rather than disintegration. Since drug absorption and physiological availability depend on having the drug in a dissolved state, suitable dissolution characteristics are an important property of a satisfactory tablet. Like the disintegration test, the dissolution test for measuring the time required for a given percentage of the drug substances in a tablet to go into solution under a specified set of conditions is an in vitro test. It is intended to provide a step towards the evaluation of the physiological availability of the drug.

STABILITY

The stability of the drug substances is investigated when developing the formulation. A suitable method of preparation must be chosen for the tableting of sensitive substances. The stability control proceeds after production by periodic examination of a stored reference sample of production batches. Tablets generally have a long shelf life. The physio-chemical properties of the tablet should also be studied during storage.

METHODS OF PREPARATION OF TABLETS

Wet granulation

The most widely use and most general method of tablet preparation is the wet granulation method. Wet granulation is a process of adding a liquid binder or adhesive to the powder mixture. The amount of liquid can be properly managed, and overwetting will cause the granules to be too hard and under wetting will cause them to be too soft and friable. Aqueous solutions have the advantage of being safer to deal with than solvents.

The procedure of Wet Granulation:

Step 1: Weighing and Blending - the active ingredient, filler, disintegration agents, are weighed and mixed.

Step 2: The wet granulate is prepared by adding the liquid binder/adhesive. Examples of binders/adhesives include aqueous preparations of corn starch, natural gums such as acacia, and cellulose derivatives such as methylcellulose.

Step 3: Screening the damp mass into pellets or granules

Step 4: Drying the granulation

Step 5: Dry screening: After the granules are dried, pass through a screen of a smaller size than the one used for the wet mass to select granules of uniform size to allow even fill in the die cavity.

Step 6: Lubrication- A dry lubricant, anti-adherent, and glidant are added to the granules either by dusting over the spread-out granules or by blending with the granules. It reduces friction between the tablet and the walls of the die cavity. Anti-adherent reduces sticking of the tablet to the die and punch.

Table No. 1: Ratios of polymers used in the formulations

BATCH	FORMULATION	CASHEW GUM	XANTHAN GUM	HPMC
1	C	100		
2	X		100	
3	H			100
4	H8C2	20		80
5	H6C4	40		60
6	H2C8	80		20
7	X8H2		80	20
8	X6H4		60	40
9	X2H8		20	80
10	X8C2	20	80	
11	X6C4	40	60	
12	X2C8	80	20	
13	C6X2H2	60	20	20
14	H6X2C2	20	20	60
15	X6C2H2	20	60	20

KEY: C – Cashew gum, X – Xanthan gum and H – Hydroxypropyl Methylcellulose (HPMC)

RESULT AND DISCUSSION:

FLOW PROPERTIES OF DICLOFENAC SODIUM GRANULES

Table No. 2: Bulk density measurements of diclofenac sodium granules prepared

Batch No	Loose bulk density	Tapped bulk density	Hausner's	Compressibility	Angle of repose
	g/mL	g/mL	Ratio	Index (%)	(º)
1	0.56	0.59	1.05	5.1	30.80 ± 0.006
2	0.45	0.48	1.07	6.3	32.41 ± 0.012
3	0.45	0.5	1.11	10.0	28.55 ± 0.026
4	0.50	0.53	1.06	5.7	31.50 ± 0.076
5	0.50	0.56	1.12	10.7	27.11 ± 0.113
6	0.48	0.5	1.04	4.0	35.30 ± 0.006
7	0.45	0.5	1.11	10.0	26.41 ± 0.017
8	0.50	0.56	1.12	10.7	29.60 ± 0.115
9	0.48	0.53	1.10	10.4	31.74 ± 0.092
10	0.53	0.59	1.11	10.2	30.20 ± 0.010
11	0.48	0.53	1.10	9.4	34.86 ± 0.029
12	0.53	0.59	1.11	10.2	25.90 ± 0.012
13	0.53	0.56	1.06	5.3	33.42 ± 0.006
14	0.45	0.5	1.11	10.0	30.65 ± 0.010
15	0.53	0.56	1.06	5.3	32.15 ± 0.026

COMPRESSION OF DICLOFENAC SODIUM MATRIX TABLETS

Tablet weight = 420 mg

Number of Tablets = 80 tablets per batch (15 batches in all) Practical yield = 958 tablets

QUALITY CONTROL TESTS CARRIED OUT ON TABLETS

Uniformity of weight

Calculation

The percentage deviations of the tablets from the mean were calculated using: Percentage deviation =

$$\frac{A - B \times 100}{B},$$

Where, A= Initial weight of tablets, B = Average weight of 20 tablets

Table No. 3: Uniformity of weight of the batches of diclofenac sodium matrix tablets

Batch No.	Total tablet weight (g)	Average weight (g) ± SD	Max % deviation	Inference
1	8.814	0.441 ± 0.012	4.833	passed
2	8.666	0.433 ± 0.007	2.977	passed
3	8.337	0.417 ± 0.011	4.893	passed
4	8.557	0.428 ± 0.009	4.021	passed
5	8.564	0.428 ± 0.011	4.52	passed
6	8.507	0.425 ± 0.011	4.372	passed
7	8.388	0.419 ± 0.012	3.672	passed
8	8.487	0.424 ± 0.011	4.689	passed
9	8.553	0.428 ± 0.012	4.139	passed
10	8.342	0.417 ± 0.010	4.363	passed
11	8.317	0.416 ± 0.012	3.175	passed
12	8.350	0.418 ± 0.009	4.335	passed
13	8.625	0.431 ± 0.010	3.617	passed
14	8.159	0.408 ± 0.009	3.137	passed
15	8.345	0.417 ± 0.011	3.209	passed

CRUSHING STRENGTH (HARDNESS)

Table No. 4: Crushing strength of the diclofenac sodium matrix tablets

Batch Number	Mean force applied (Kg)
1	4.4 ± 1.11
2	6.8 ± 1.60
3	3.8 ± 0.75
4	4.0 ± 0.81
5	4.0 ± 0.77
6	4.1 ± 1.22
7	4.1 ± 0.65
8	4.3 ± 0.64
9	5.2 ± 1.18
10	4.1 ± 0.83
11	5.3 ± 1.91
12	4.0 ± 0.63
13	4.1 ± 0.70
14	6.6 ± 1.85
15	5.7 ± 1.72

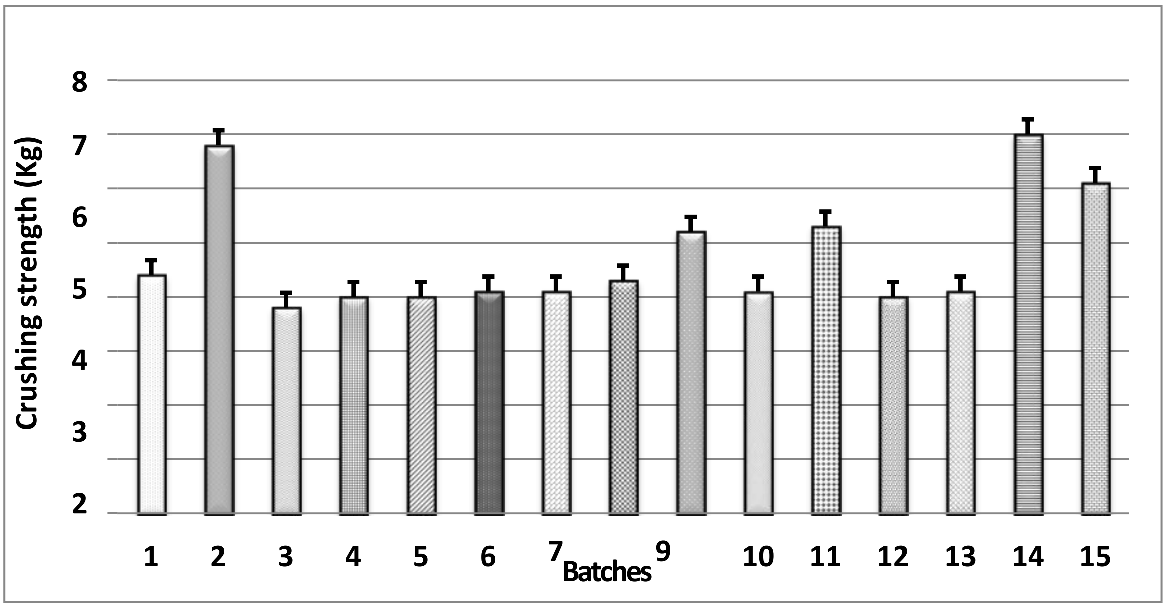

Figure No. 2: Crushing strength of the diclofenac sodium matrix tablets

FRIABILITY

Table No. 5: Friability of the diclofenac sodium matrix tablets

Batch	Initial weight (Wi)	Final weight (Wf)	Weight loss	% loss
1	6.01	5.95	0.06	1.00
2	6.28	6.27	0.01	0.16
3	6.28	6.24	0.04	0.64
4	6.36	6.29	0.07	1.10
5	6.35	6.30	0.05	0.79
6	6.36	6.33	0.03	0.47
7	6.31	6.30	0.01	0.16
8	6.29	6.24	0.05	0.80
9	6.36	6.32	0.04	0.63
10	6.19	6.11	0.08	1.30
11	6.19	6.14	0.05	0.81
12	6.2	6.19	0.01	0.16
13	6.1	6.09	0.01	0.16
14	6.12	6.08	0.04	0.65
15	6.05	6.01	0.04	0.66

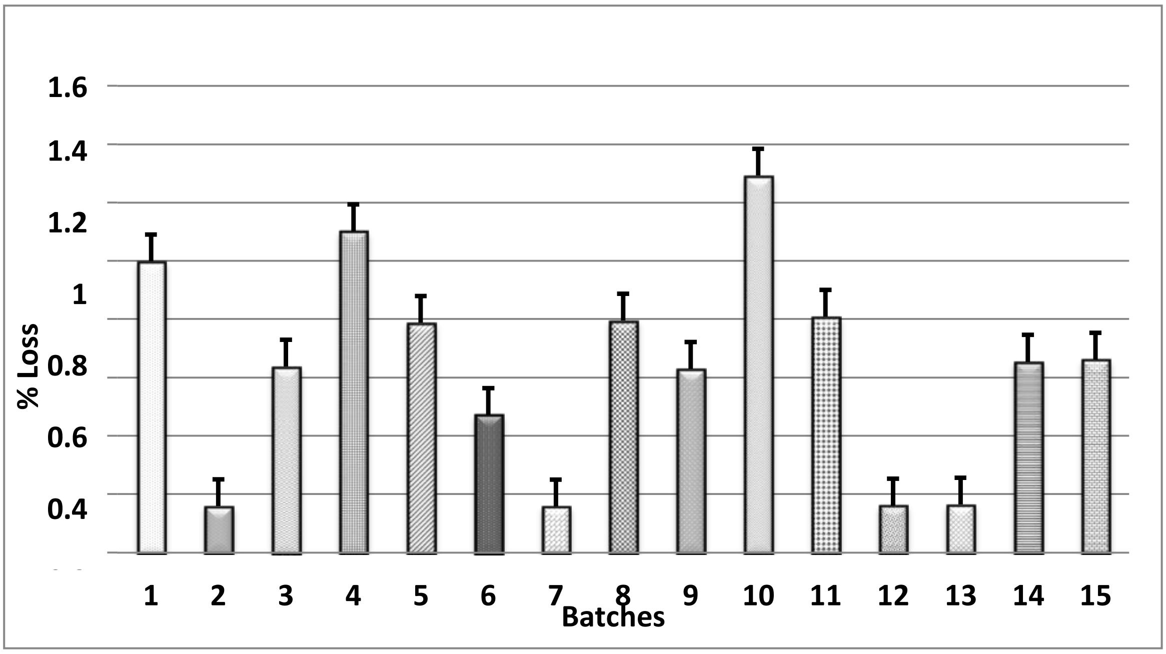

Figure No. 3: Friability of the diclofenac sodium matrix tablets

DISSOLUTION PROFILE OF DICLOFENAC SODIUM TABLETS FORMULATED WITH DIFFERENT GUMRATIOS

Calibration curve for diclofenac sodium in phosphate buffer pH 7.5 at a wavelength of 276 nm

Blank used: Phosphate buffer, pH 7.5

Table No. 6: Absorbance of pure Diclofenac Sodium in Phosphate buffer pH 7.5

Concentration (%w/v)	Absorbance
0.00250	0.760
0.00150	0.438
0.00125	0.356
0.00100	0.274
0.00075	0.165

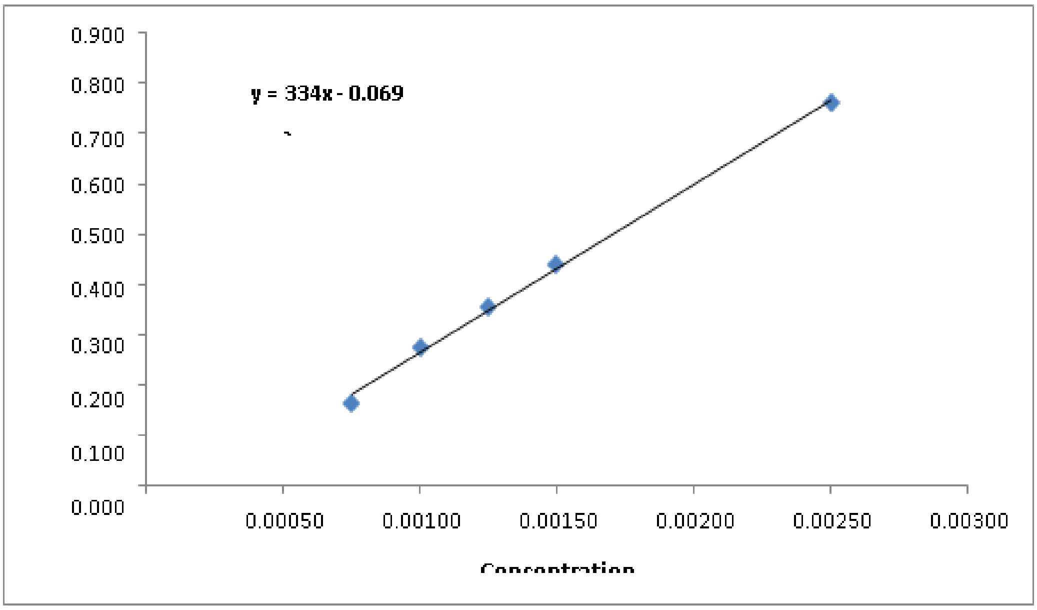

Figure No. 4: Calibration curve for diclofenac sodium in phosphate buffer pH 7.5

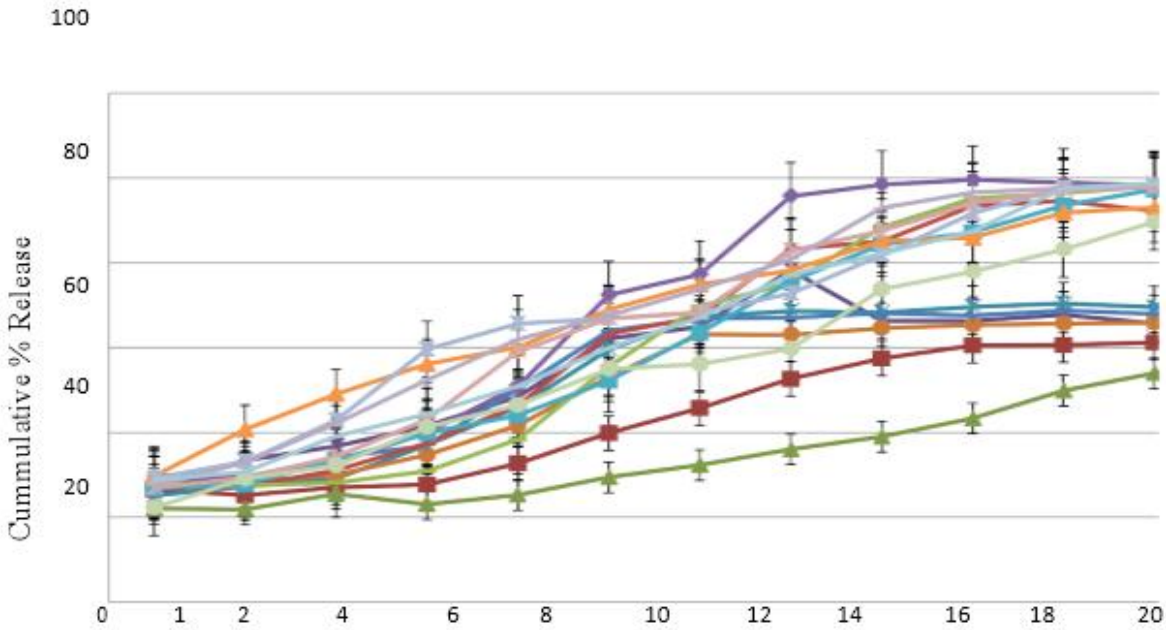

Figure No. 5: Cummulative % Release of Diclofenac Sodium of All Batches

MECHANISM AND RELEASE KINETICS OF THE DICLOFENAC SODIUM MATRIXTABLETS

Table No. 7: Mechanism and release kinetics of the diclofenac sodium matrix tablets produced

	Zero Order		First Order		Higuchi		Hixson-Crowell	
Batch No	**K_o**	**R^2**	**K_1**	**R^2**	**K_H**	**R^2**	**K_{HC}**	**R^2**
1	0.0278	0.8107	0.0006	0.7088	1.2050	0.9325	0.0012	0.748
2	0.0273	0.9880	0.0009	0.8257	1.0842	0.9563	0.0015	0.909
3	0.0237	0.5265	0.0004	0.4700	1.1279	0.7310	0.0009	0.498
4	0.0298	0.6313	0.0005	0.5209	1.3794	0.8308	0.0011	0.562
5	0.0268	0.6664	0.0005	0.5854	1.2228	0.8542	0.0010	0.615
6	0.0257	0.5913	0.0004	0.5221	1.2023	0.7952	0.0009	0.547
7	0.0493	0.7735	0.0006	0.6305	2.1720	0.9231	0.0015	0.687
8	0.0568	0.8392	0.0007	0.7080	2.4360	0.9493	0.0017	0.757
9	0.0507	0.6997	0.0006	0.5969	2.2861	0.8753	0.0015	0.637
10	0.0535	0.8816	0.0006	0.7068	2.2722	0.9750	0.0016	0.779
11	0.0391	0.7951	0.0004	0.5752	1.7170	0.9404	0.0010	0.659
12	0.0465	0.8247	0.0005	0.5978	1.9622	0.9373	0.0012	0.682
13	0.0513	0.8119	0.0006	0.6147	2.2378	0.9497	0.0015	0.689
14	0.0479	0.9147	0.0007	0.5975	2.0062	0.9873	0.0015	0.741
15	0.0475	0.7863	0.0005	0.5748	2.0901	0.9363	0.0013	0.657

SUMMARY AND CONCLUSION:

- Cashew gum can be purified to achieve a good yield.
- Both cashew and xanthan gums showed pseudoplastic flow.
- All the batches of tablets passed the uniformity of weight test and drug content test.
- All the batches of tablets but batch 3 passed the crushing strength test.
- All the batches of tablets but batches 4 and 10 passed the friability test.
- Tablets containing only xanthan gum as release modifier achieved the highest crushing strength friability ratio (CSFR) with those in batch 10 having the lowest.
- Tablets in batch 2 had the highest swelling index and those in batch 3 had the lowest swelling index.
- The study has shown that cashew and xanthan gums used alone cannot efficiently control

drug release.

- Batches 7 and 8 containing xanthan gum and HPMC was able to cause sustained drug release comparable to Voltaren Retard.

- The formulation containing xanthan and cashew gums in batches 10, 11, 12 showed good sustained-release properties similar to the reference sample.

- Batches 13 and 15 which contained all three combinations were also able to provide sustained drug release similar to Voltaren Retard.

- The release profile fit the Higuchi equation better than the rest thus drug may have been released through the Higuchi model of drug kinetics.

- The release exponent 'n' determined was between 0.45 and 0.89 thus the drug is released through anomalous or non – Fickian diffusion.

FUTURE RECOMMENDATIONS:

- Fourier Transform–Infra-Red (FT-IR) spectroscopy can be employed to evaluate the compatibility of the drug and the polymers used.

- *In-vivo* studies should be performed to ascertain the effectiveness of the formulations.

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